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Ambient Water Quality Criteria: Aldrin/Dieldrin

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ALDRIN/DIELDRIN

Ambient Water Quality Criteria

Criteria and Standards Division
Office of Water Planning and Standards
U.S. Environmental Protection Agency
Washington, D.C.

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Criteria and Standards Div.

Section 304(a) of the Clean Water Act (33 U.S.C. 1314(a)), requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for aldrin and dieldrin. It presents concentration criteria for the protection of fresh water and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A section 304(a) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and in its,...

KEYWORDS: *Aldrin, *Water quality, *Toxicology, *Dieldrin, *Pesticides, *Toxic substances, *Water pollution effects(Humans).

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March 23, 1979

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CRITERION DOCUMENT

ALDRIN-DIELDRIN

CRITERIA

Aquatic Life

For aldrin/dieldrin the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0019 µg/l as a 24-hour average and the concentration should not exceed 1.2 µg/l at any time.

For aldrin/dieldrin the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 0.0069 µg/l as a 24-hour average and the concentration should not exceed 0.16 µg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to aldrin through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of aldrin estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Critrion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 4.6×10^{-2} ng/l, 4.6×10^{-3} ng/l, and 4.6×10^{-4} ng/l, respectively.

For the maximum protection of human health from the potential carcinogenic effects of exposure to dieldrin through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of dieldrin estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 4.4×10^{-2} ng/l, 4.4×10^{-3} ng/l, and 4.4×10^{-4} ng/l respectively.

Introduction

Aldrin and dieldrin have been two of the most widely used domestic pesticides. They are chlorinated hydrocarbon compounds. Although aldrin is used in greater quantity than dieldrin, aldrin quickly transforms into dieldrin in the environment. Hence, there is concern with both compounds. The primary use of the chemicals in the past was for control of corn pests, although they were also used by the citrus industry. Uses are restricted to those where there is no effluent discharge.

Aldrin use in the United States peaked at 19 million pounds in 1966 but dropped to about 10.5 million pounds in 1970. During that same period dieldrin use decreased from 1 million pounds to about 670,000 pounds. The decreased use has been attributed primarily to increased insect resistance to the two chemicals and to development and availability of substitute materials.

Aldrin and dieldrin have been the subject of litigation bearing upon the contention that these substances cause severe aquatic environmental change and are potential carcinogens. In 1970, the U.S. Department of Agriculture cancelled all registrations of these pesticides based upon a concern to limit dispersal in or on aquatic areas. In 1972, under the authority of the Fungicide, Insecticide, Rodenticide Act as amended by the Federal Pesticide Control Act of 1972, USCS Section 135, et. sec., an EPA order lifted cancellation of all registered aldrin and dieldrin for use in deep ground insertions for termite control, nursery clipping of roots and tops of non-food plants, and mothproofing of woolen textiles and carpets where there is no effluent discharge. In 1974, cancellation proceedings disclosed the severe hazard to human health and suspension of registration of aldrin and dieldrin use was ordered; production was restricted for all pesticide products containing aldrin or dieldrin. However, formulated products containing aldrin and dieldrin are imported from Europe each year solely for subsurface soil injection for termite control. Therefore, limits that protect all receiving water uses must be placed on aldrin and dieldrin. The litigation has produced the evidentiary basis for the Administrator's conclusions that aldrin/dieldrin are carcinogenic in mice and rats, approved the Agency's extrapolation to humans of data derived from tests on animals, and affirmed the conclusions that aldrin and dieldrin pose a substantial risk of cancer to humans, which constitutes an "imminent hazard" to man.

Aldrin and dieldrin are white crystalline substances with aldrin melting at 104°C and dieldrin melting between 176 to 177°C. Both are soluble in organic solvents with dieldrin the least soluble of the two. The chemical name for aldrin is 1, 2, 3, 4, 10, 10-hexachloro-1, 4, 4a, 5, 8, 8a-hexahydro-1, 4: 5, 8-exo-dimethanonaphathalene. The chemical name for dieldrin is 1, 2, 3, 4, 10, 10-hexachloro-6, 7-epoxy-1, 4, 4a, 5, 6, 7, 8, 8a-octahydro-endo, exo-1, 4: 5, 8-dimethanonaphthalene.

Aldrin is metabolically converted to dieldrin. This epoxidation has been shown to occur in several species including mammals and poultry, houseflies, locusts, soil microorganisms, a large number of Lepidoptera species, freshwater fish (Gakstatter, 1968), and a number of freshwater invertebrates including protozoa, coelenterates, worms, arthropods, molluscs, and lobsters. The aldrin molecule is biologically altered in the environment to a more stable and at least equally toxic form, dieldrin. Dieldrin is known to be metabolically degraded as shown by Matsumura and Boush (1967) and Patil, et al. (1972); however, its persistence in the environment is due to its extremely low volatility (i.e., a vapor pressure of 1.78 x 10-7 mm mercury at 20°C) and low solubility in water (186 µg/l at 25 to 29°C) (Int. Agency Res. Cancer, 1974). In addition, dieldrin is extremely apolar, resulting in a high affinity for fat which accounts for its retention in animal fats, plant waxes, and other such organic matter in the environment. The fat solubility of dieldrin results in the progressive accumulation in the food chain which may result in a concentration in an organism which would exceed the lethal limit for a consumer.

Many organisms not in direct contact with contaminated water and sediment accumulate aldrin/dieldrin from the food supply. This biological concentration results in tissue concentrations many times those found in the surrounding environment (Sanborn and Yu, 1973). Concentrations increase in the food chain reaching the carnivores at the top including man.

Dieldrin is probably the most stable insecticide among the cyclodienes (i.e., isodrin-endrin; heptaclor-heptachlor epoxide). The time required for 95 percent of the dieldrin to disappear from soil has been estimated to vary from 5 to 25 years depending upon the microbial flora of the soil

(Edwards, 1966). Dieldrin applied at 100 ppm has been shown to persist in soil for more than six years (Westlake and San Antonio, 1960), while at 25 ppm in a different soil type, a 50 percent loss was found at seven years (Nash and Woolson, 1967). When applied to sandy soil at a rate of 100 ppm, residues could be found 15 years later. Matsumura and Boush (1967) found that of 577 bacterial isolates collected from areas heavily contaminated with dieldrin, 10 isolates would alter dieldrin to two to nine unidentified metabolites. The microbes were members of Pseudomonas, Bacillus, and Trichoderma genera. Subsequent microbiological studies by Wedemeyer (1968) revealed that Aerobacter aerogenes also will alter dieldrin similarly to 6,7- trans-dihydroxydihydroaldrin. Chacko, et al. (1966) tested this capability of 17 species of fungi and actinomycetes. Though most degraded pentachloronitrobenzene (PCNE) or DDT or both, none degraded dieldrin.

Patil, et al. 1972, studied the metabolic transformations of aldrin/dieldrin by marine algae, surface film, sediments, and water. They found that the insecticide was not degraded or metabolized in sea water or polluted waters. Some marine algal populations were shown to degrade aldrin to dieldrin.

Alterations of dieldrin by bacterial systems result in the formation of at least one acidic product (Matsumura and Boush, 1967). Once in the fatty tissue of organisms, dieldrin remains stable, according to Sanborn and Yu (1973). However, dieldrin can be mobilized from fatty tissue as demonstrated by Brockway (1973); for example, when fish are placed in an environment without dieldrin, there is an elimination from the tissue (Brockway, 1973). The elimination rate depends upon the diet with fasted fish eliminating dieldrin more rapidly than fed fish because of the utilization of fat stores (Grzenda, et al. 1972).

The dieldrin eliminated from the tissues reenters the water and thus becomes available for bioconcentration by other organisms. The movement of dieldrin among organisms, water, and sediment is dynamic, with equilibrium attained when the chemical concentration is constant.

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AQUATIC LIFE TOXICOLOGY*

FRESHWATER ORGANISMS

Introduction

Aldrin and dieldrin are members of a group of synthetic cyclic hydrocarbons called cyclodienes. The group includes other insecticides such as chlordane, heptachlor, endosulfan and endrin. Until recently, aldrin and dieldrin were the most widely used domestic pesticides with aldrin being applied in much greater quantities than dieldrin. However, these pesticides are often considered together since aldrin is rapidly converted in animal or plant tissue and soil to dieldrin. This conversion is accomplished through the addition of an epoxide group to the aldrin molecule.

Since aldrin is rapidly converted to dieldrin and there are no adequate data in all the criterion areas, no criterion has been developed for aldrin. The following discussion is based on dieldrin data only except where specifically noted.

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life [43 FR 21506 (May 18, 1978) and 43 FR 29028 (July 5, 1978)] in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are the calculations for deriving various measures of toxicity as described in the Guidelines.

Acute Toxicity

Sixty-seven acute toxicity tests using dieldrin are reported in Table 1. The tests were conducted with ten species of fish ranging from coldwater fish such as the rainbow trout, coho and chinook salmon to warmwater fish such as the goldfish and carp. All of the tests were static and none included measured concentrations. The adjustment of a 48-hour LC50 to a 96-hour value was necessary only for the exposure of the mosquitofish.

Dieldrin is acutely toxic at low concentrations. Only 10 of the 67 adjusted LC50 values are greater than 10 µg/l and a majority of the values below 10 µg/l are in the range of 0.6 to 5.5 µg/l. There are, however, species differences. The most sensitive fish tested was the rainbow trout with 96-hour LC50 values between 0.6 µg/l and 5.4 µg/l. The other salmonids (coho and chinook salmon) had 96-hour LC50 values of 3.3 and 5.9 µg/l, respectively. The most resistant fishes were the carp and the goldfish with 96-hour LC50 values of 33 and 22 µg/l, respectively. In the middle of the range, between the salmonids and the carp, were fathead minnows (range 9 to 20 µg/l) and the bluegill (range 4.8 to 17 µg/l). Special attention should be given to the data on the guppy in the report by Chadwick and Kiigemagi (1968) concerning the development of a toxicant delivery system. To determine the efficiency of the system, guppy toxicity tests were conducted over an extended time period and the data are included in Table 1. Thirty-eight of the 67 test results are from this study and range from 1.3 to 5.5 µg/l.

Thirteen fish species were tested and 23 tests were completed using aldrin. The range of the adjusted values (1.2 to

25.1 µg/l) is similar to the values obtained for dieldrin. One test, not included in the range, had a 96-hour LC50 value of 97 µg/l. This test used the mosquitofish which is well-known for pesticide-resistant wild populations. When the geometric means from Table 1 are divided by the sensitivity factor 3.9, the resulting Final Fish Acute Values are 1.6 and 2.4 µg/l for dieldrin and aldrin, respectively. Only 11 of the 67 dieldrin tests are lower than this concentration (1.6 µg/l) and of these 11, 8 are with the guppy (Chadwick and Kiigemagi, 1968) and are balanced by 30 values above 1.6 µg/l. The other three LC50 values are for the rainbow trout. These results suggest that the adjustment factors from the Guidelines are appropriate.

Nineteen acute toxicity test results for dieldrin and invertebrate species are presented in Table 2. All of these tests were conducted under static water conditions and the concentra- tions were not measured. The adjusted concentrations range from a 96-hour LC50 value of 0.4 µg/l for the stoneflies Pteronarcella badia and Pteronarcys californica (Sanders and Cope, 1968) to 627 µg/l for the crayfish (Sanders, 1972). This wide range in concentration of over 1,500 times demonstrates definite differences in interspecific sensitivity to this compound.

Intraspecific variation is apparent for the stonefly and ostracod data. This variation may have resulted from differences in experimental procedures used in stonefly testing and Guideline applications to the ostracod data. Sanders and Cope (1968) determined a 96-hour LC50 value of 0.5 µg/l dieldrin at 15°C for the stonefly Pteronarcys californica. They did not aerate the test water. Jenson and Gaufin (1964) used aeration and a slightly higher test temperature of 15.5°C and determined a much larger (about 78 times) 96-hour LC50 value of 39 µg/l for this species. Since this insect inhabits well oxygenated flowing water the non-aerated static test may have potentiated toxic effects. Hansen and Kawatski (1976) report a 24-hour LC50 value of 185 µg/l and a 72-hour LC50 value of 12.3 µg/l with the ostracod Cypretta kawatai. These tests were conducted under similar conditions but were of different duration.

The geometric mean of the dieldrin data, 26 µg/l, was divided by the sensitivity factor of 21 from the Guidelines to obtain a concentration of 1.2 µg/l. This concentration is higher than 3 of the 19 adjusted concentrations for the tested invertebrate species; this result appears to support the procedures in the Guidelines for the sensitivity factor.

Results of 13 acute toxicity tests with aldrin are also presented in Table 2. Each test was conducted so that data could be compared with data obtained from similar tests with dieldrin. Adjusted aldrin 96-hour LC50 values range from 1.1 µg/l for the stonefly (Sanders and Cope, 1968) to 32,609 µg/l for the scud (Gaufin, et al. 1965). The cladocerans were relatively more sen- 1966). In all other cases the invertebrates were relatively more sensitive to dieldrin. For aldrin, the estimated concentration at or below the 96-hour LC50 value for 95 percent of all invertebrate species is 3.8 µg/l.

Acute toxicity tests with aldrin and dieldrin have established that these compounds are toxic to aquatic life at low concentrations. The data indicate that dieldrin is slightly more toxic than aldrin for both fish and invertebrates. The Final Fish

Acute Value is 1.6 µg/l and the Final Invertebrate Acute Value is 1.2 µg/l. Because the Invertebrate Acute Value is the lowest, the Final Acute Value is 1.2 µg/l.

Chronic Toxicity

Two chronic toxicity tests have been conducted with dieldrin. One was an embryo-larval exposure using steelhead (rainbow) trout (Chadwick and Shumway, 1969). This species was the most sensitive species according to the acute studies (Table 1). The other chronic exposure was a three-generation study using the guppy (Roelofs, 1971). Fortunately, the 96-hour LC50 concentration is well-established for this fish (Table 1) and is about 2.9 µg/l. The geometric mean (0.21 µg/l) of the two chronic concentrations divided by the sensitivity factor (6.7) results in a 95 percent protection concentration or Final Fish Chronic Value of 0.031 µg/l (Table 3). Since the two tested species include the most sensitive and a moderately sensitive species, the calculated concentration should confer adequate protection for the non-tested fish species.

No chronic studies were found for these important animals. Because of the lack of chronic data, it is necessary to reexamine the invertebrate test results. All of the acute invertebrate values are greater than the fish geometric mean chronic concentration of 0.21 µg/l. However, three stonefly species have adjusted acute values (0.4 to 0.5 µg/l) which are close to the fish geometric mean value. These data were obtained under static water conditions without aeration and the dieldrin concentrations were not measured. More meaningful data for assessing the risk of chronic exposure of dieldrin to stoneflies was obtained by Jensen and

Gaufin (1966). They determined a 30-day LC50 value of 2 µg/l, based on measured concentrations, for one of the three species, *P. californica* (Table 6), in flowing water to which stoneflies are adapted. A lower 30-day LC50 value of 0.2 µg/l was also obtained for another stonefly *Acroneuria pacifica*. These data indicate that the insect chronic value might be less than that calculated for fish. A lower value might be expected because the primary use of dieldrin was as an insecticide.

After applying the sensitivity factor the Final Fish Chronic Value is 0.031 µg/l. The extent of protection for the invertebrates is unknown but it can be estimated from the acute toxicity test that many would be safe if exposed at the concentration of 0.031 µg/l.

Plant Effects

Four dieldrin toxicity tests using three plant species were found (Table 4). The alga, *Scenedesmus quadricaudata*, was the most sensitive species tested with a 22 percent reduction in biomass after exposure to 100 µg/l of dieldrin (Stadnyk and Campbell, 1971). The other species, diatom and water meal, were affected only at concentrations 100 times higher than the alga. Since fish and invertebrate species were affected at concentrations 100 times lower than the alga, the plants should be protected by the animal-derived data.

Residues

Table 5 contains the results of 10 residue studies with dieldrin. No comparable aldrin data were found. The 10 studies include plant, invertebrate and fish species. The range of the bioconcentration factors (BCF) are from 128 for an alga (Reinert,

1972) to 68,286 for lake trout (Reinert, et al. 1974). All of the authors (except Reinert, et al. 1974) indicate that an equilibrium had occurred in their specific study. An examination of the data in the reports supports the conclusion of the individual authors.

The analysis of the residue data can be divided into two broad groups, the plant-invertebrate and the fish data. The plant-invertebrate BCF values range from 128 to 5,558. The two values representing the algal and diatom community accumulations are perhaps the most ecologically applicable data in this group. The studies were conducted in open channels under field conditions whereas the other algal study was a short-exposure laboratory test. The invertebrate BCF values show a comparatively low bioaccumulation potential for the two species.

The fish BCF values range from 2,385 to 68,286. Although all but one of the authors report that equilibrium had occurred in each of their exposures, there seems to be a relationship between length of exposure and total residue accumulation. For example, guppies exposed for 32 days had a BCF of 12,708 while exposure for 160 to 230 days resulted in a BCF of 28,408. The same relationship may explain the high BCF for the lake trout. The bioconcentration of dieldrin by this species may become greater since the fish had not reached an equilibrium when the study was terminated. The channel catfish BCF is the lowest of the fish values (Shannon, 1977a,b). This is probably a result of the experimenter analyzing dorsal muscle rather than whole fish as was done by the others.

The residue limit established by the Food and Drug Administration (FDA) for dieldrin in domestic animal feed is 0.03 mg/kg, and was used to calculate the Residue Limited Toxicant Concentration (RLTC). The FDA domestic animal feed concentration of 0.03 mg/kg divided by the average fish bioconcentration factor of 15,482 gives a RLTC of 0.0000019 mg/kg or 0.0019 µg/l.

The lowest of the Final Fish Chronic Value (0.031 µg/l), Final Invertebrate Chronic Value (none), Final Plant Value (100 µg/l) and the RLTC (0.0019 µg/l) is used to determine the Final Chronic Value. For dieldrin the Final Chronic Value is 0.0019 µg/l.

Miscellaneous

Data presented in Table 6 do not conflict with the selection of 0.0019 µg/l as the Final Chronic Value.

CRITERION FORMULATION

Freshwater-Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value = 1.6 μg/l

Final Invertebrate Acute Value = 1.2 μg/l

Final Acute Value = 1.2 μg/l

Final Fish Chronic Value = 0.031 μg/l

Final Invertebrate Chronic Value = not available

Final Plant Value = 100 μg/l

Residue Limited Toxicant Concentration = 0.0019 μg/l

Final Chronic Value = 0.0019 μg/l

0.44 x Final Acute Value = 0.53 μg/l

The maximum concentration of dieldrin is the Final Acute Value of 1.2 μg/l which is based on the more acutely sensitive invertebrate organisms. Since 0.44 times the Final Acute Value (0.44 x 1.2 μg/l = 0.53 μg/l) is not lower than the Final Chronic Value (0.0019 μg/l), the latter is the recommended 24-hour average concentration. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For dieldrin the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0019 μg/l as a hour 24-average and the concentration should not exceed 1.2 μg/l at any time.

Table 1. Freshwater fish acute values for aldrin/dieldrin

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
			Dieldrin				
Rainbow trout, *Salmo gairdneri*	S	U	90% dieldrin	96	9.9	5.4	Katz, 1961
Rainbow trout, *Salmo gairdneri*	S	U	85% dieldrin	96	2.4	1.3	Macek, et al. 1969
Rainbow trout, *Salmo gairdneri*	S	U	85% dieldrin	96	1.1	0.6	Macek, et al. 1959
Rainbow trout, *Salmo gairdneri*	S	U	85% dieldrin	96	1.4	0.8	Macek, et al. 1969
Coho salmon, *Oncorhynchus kisutch*	S	U	90% dieldrin	96	10.8	5.9	Katz, 1961
Chinook salmon, *Oncorhynchus tshawytscha*	S	U	90% dieldrin	96	6.1	3.3	Katz, 1961
Goldfish, *Carassius auratus*	S	U	90% dieldrin	96	41	22	Henderson, et al. 1959
Carp, *Cyprinus carpio*	S	U	15% dieldrin	96	60	33	Rao, et al. 1975
Fathead minnow, *Pimephales promelas*	S	U	90% dieldrin	96	18	10	Henderson, et al. 1959
Fathead minnow, *Pimephales promelas*	S	U	90% dieldrin	96	18	10	Henderson, et al. 1959
Fathead minnow, *Pimephales promelas*	S	U	85% dieldrin	96	36	20	Tarzwell Henderson, 1957
Fathead minnow, *Pimephales promelas*	S	U	85% dieldrin	96	24	13	Tarzwell & Henderson, 1957
Fathead minnow, *Pimephales promelas*	S	U	85% dieldrin	96	16	9	Tarzwell & Henderson, 1957
Fathead minnow, *Pimephales promelas*	S	U	85% dieldrin	96	25	14	Tarzwell & Henderson, 1957

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Fathead minnow, *Pimephales promelas*	S	U	85% dieldrin	96	23	13	Tarzwell & Henderson, 1957
Mosquitofish, *Gambusia affinis*	S	U	95% dieldrin	48	8	3	Culley & Ferguson, 1969
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	3.9	2.1	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	4.7	2.6	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	3.9	2.1	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	5.1	2.8	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	3.9	2.1	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	3.7	2.0	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	3.2	1.7	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	3.9	2.1	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	4.2	2.3	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	4.3	2.3	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	4.3	2.3	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	4.1	2.2	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	3.5	1.9	Chadwick & Kiigemagi, 1968

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	4.7	2.6	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	3.2	1.7	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	2.9	1.6	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	2.6	1.4	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	2.9	1.6	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	2.4	1.3	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	2.6	1.4	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	2.3	1.3	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	2.7	1.5	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	2.3	1.3	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	2.7	1.5	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	2.7	1.5	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	4.8	2.6	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	6.1	3.3	Chadwick & Kiigemagi, 1968
Guppy, *Poecilia reticulata*	S	U	Technical grade dieldrin	96	3.2	1.7	Chadwick & Kiigemagi, 1968

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Guppy, Poecilia reticulata	S	U	99+% dieldrin	96	6.6	3.6	Chadwick & Kiigemagi, 1968
Guppy, Poecilia reticulata	S	U	99+% dieldrin	96	5.6	3.1	Chadwick & Kiigemagi, 1968
Guppy, Poecilia reticulata	S	U	99+% dieldrin	96	6.1	3.3	Chadwick & Kiigemagi, 1968
Guppy, Poecilia reticulata	S	U	99+% dieldrin	96	7.5	4.1	Chadwick & Kiigemagi, 1968
Guppy, Poecilia reticulata	S	U	99+% dieldrin	96	10	5.5	Chadwick & Kiigemagi, 1968
Guppy, Poecilia reticulata	S	U	99+% dieldrin	96	6.6	3.6	Chadwick & Kiigemagi, 1968
Guppy, Poecilia reticulata	S	U	99+% dieldrin	96	6.6	3.6	Chadwick & Kiigemagi, 1968
Guppy, Poecilia reticulata	S	U	99+% dieldrin	96	6.9	3.8	Chadwick & Kiigemagi, 1968
Guppy, Poecilia reticulata	S	U	99+% dieldrin	96	4.7	2.6	Chadwick & Kiigemagi, 1968
Guppy, Poecilia reticulata	S	U	99+% dieldrin	96	7.5	4.1	Chadwick & Kiigemagi, 1968
Guppy, Poecilia reticulata	S	U	90% dieldrin	96	25	14	Henderson, et al. 1959
Guppy, Poecilia reticulata	S	U	Dieldrin	96	21	11	Cairns & Loos, 1966
Green sunfish, Lepomis cyanellus	S	U	85% dieldrin	96	6	3	Tarzwell & Henderson, 1957
Green sunfish, Lepomis cyanellus	S	U	85% dieldrin	96	11	6	Tarzwell & Henderson, 1957
Green sunfish, Lepomis cyanellus	S	U	85% dieldrin	96	8	4	Tarzwell & Henderson, 1957

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Bluegill, *Lepomis macrochirus*	S	U	90% dieldrin	96	9	5	Henderson, et al. 1959
Bluegill, *Lepomis macrochirus*	S	U	85% dieldrin	96	17	9	Macek, et al. 1969
Bluegill, *Lepomis macrochirus*	S	U	85% dieldrin	96	14	8	Macek, et al. 1969
Bluegill, *Lepomis macrochirus*	S	U	85% dieldrin	96	8.8	4.8	Macek, et al. 1969
Bluegill, *Lepomis macrochirus*	S	U	85% dieldrin	96	32	17	Tarzwell & Henderson, 1957
Bluegill, *Lepomis macrochirus*	S	U	85% dieldrin	96	18	10	Tarzwell & Henderson, 1957
Bluegill, *Lepomis macrochirus*	S	U	85% dieldrin	96	8	4	Tarzwell & Henderson, 1957
Bluegill, *Lepomis macrochirus*	S	U	85% dieldrin	96	22	12	Tarzwell & Henderson, 1957
			Aldrin				
American eel, *Anguilla rostrata*	S	U	Aldrin	96	16	9	Rehwoldt, et al. 1977
Rainbow trout, *Salmo gairdneri*	S	U	88.4% aldrin	96	17.7	9.7	Katz, 1961
Rainbow trout, *Salmo gairdneri*	S	U	95% aldrin	96	3.2	1.7	Macek, et al. 1969
Rainbow trout, *Salmo gairdneri*	S	U	95% aldrin	96	3.3	1.8	Macek, et al. 1969
Rainbow trout, *Salmo gairdneri*	S	U	95% aldrin	96	2.2	1.2	Macek, et al. 1969
Coho salmon, *Oncorhynchus kisutch*	S	U	88.4% aldrin	96	45.9	25.1	Katz, 1961

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Chinook salmon, Oncorhynchus tshawytscha	S	U	88.4% aldrin	96	6.1	3.3	Katz, 1961
Goldfish, Carassius auratus	S	U	88.4% aldrin	96	32	17	Henderson, et al. 1959
Carp, Cyprinus carpio	S	U	30% aldrin	96	3.7	2	Rao, et al. 1975
Carp, Cyprinus carpio	S	U	Aldrin	96	[illegible]	2.2	Rehwoldt, et al. 1977
Fathead minnow, Pimephales promelas	S	U	88.4% aldrin	96	37	20	Henderson, et al. 1959
Fathead minnow, Pimephales promelas	S	U	88.4% aldrin	96	32	17	Henderson, et al. 1959
Banded killifish, Fundulus diaphanus	S	U	Aldrin	96	21	11	Rehwoldt, et al. 1977
Mosquitofish, Gambusia affinis	S	U	95% aldrin	48	36	16	Culley & Ferguson, 1969
Mosquitofish, Gambusia affinis	S	U	Aldrin	24	270	97	Krieger & Lee, 1973
Guppy, Poecilia reticulata	S	U	88.4% aldrin	96	37	20	Henderson, et al. 1959
Guppy, Poecilia reticulata	S	U	Aldrin	96	20	11	Rehwoldt, et al. 1977
White perch, Roccus americanus	S	U	Aldrin	96	42	23	Rehwoldt, et al. 1977
Striped bass, Morone saxatilis	S	U	Aldrin	96	10	7	Rehwoldt, et al. 1977
Bluegill, Lepomis macrochirus	S	U	88.4% aldrin	96	15	8	Henderson, et al. 1959
Bluegill, Lepomis macrochirus	S	U	95% aldrin	96	7.7	4.2	Macek, et al. 1969

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (µg/l)	Adjusted LC50 (µg/l)	Reference
Bluegill, *Lepomis macrochirus*	S	U	95% aldrin	96	5.8	3.2	Macek, et al. 1969
Bluegill, *Lepomis macrochirus*	S	U	95% aldrin	96	4.6	2.5	Macek, et al. 1969

* S = static

** U = unmeasured

Geometric mean of adjusted values: Dieldrin = 5.9 µg/l $\frac{5.9}{3.9} = 1.6$ µg/l

Aldrin = 9.4 µg/l $\frac{9.4}{3.9} = 2.4$ µg/l

Table 2. Freshwater intertebrate acute values for aldrin/dieldrin

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
			Dieldrin				
Cladoceran, *Daphnia carinata*	S	U	Technical grade dieldrin	48	130	110	Santharam, et al. 1976
Cladoceran, *Daphnia pulex*	S	U	Dieldrin	48	250	212	Sanders & Cope, 1966
Cladoceran, *Simocephalus serrulatus*	S	U	Dieldrin	48	240	203	Sanders & Cope, 1966
Cladoceran, *Simocephalus serrulatus*	S	U	Dieldrin	48	190	161	Sanders & Cope, 1966
Ostracod, *Cypretta kawatai*	S	U	99+% dieldrin	24	185	41	Hansen & Kawatski, 1976
Ostracod, *Cypretta kawatai*	S	U	99+% dieldrin	72	12.3	6.3	Hansen & Kawatski, 1976
Isopod, *Asellus breicaudus*	S	U	Dieldrin	96	5	4	Sanders, 1972
Scud, *Gammarus fasciatus*	S	U	Dieldrin	96	640	542	Sanders, 1972
Scud, *Gammarus fasciatus*	S	U	Dieldrin	96	600	508	Sanders, 1972
Scud, *Gammarus lacustris*	S	U	Dieldrin	96	700	593	Gaufin, et al. 1965
Scud, *Gammarus lacustris*	S	U	Dieldrin	96	460	390	Sanders, 1969
Glass shrimp, *Palaemonetes kadiakensis*	S	U	Dieldrin	96	20	17	Sanders, 1972
Crayfish, *Orconectes nais*	S	U	Dieldrin	96	740	627	Sanders, 1972
Mayfly, *Ephemerella grandis*	S	U	Dieldrin	96	8	7	Gaufin, et al. 1965

Table 2. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Stonefly, *Acroneuria pacifica*	S	U	100% dieldrin	96	24	20	Jensen & Gaufin, 1964
Stonefly, *Claassenia sabulosa*	S	U	Dieldrin	96	0.58	0.5	Sanders & Cope, 1968
Stonefly, *Pteronarcella badia*	S	U	Dieldrin	96	0.5	0.4	Sanders & Cope, 1968
Stonefly, *Pteronarcys californica*	S	U	100% dieldrin	96	39	33	Jensen & Gaufin, 1964
Stonefly, *Pteronarcys californica*	S	U	Technical grade dieldrin	96	0.5	0.4	Sanders & Cope, 1968
			Aldrin				
Cladoceran, *Daphnia pulex*	S	U	Aldrin	48	28	24	Sanders & Cope, 1966
Cladoceran, *Simocephalus serrulatus*	S	U	Aldrin	48	23	19	Sanders & Cope, 1966
Cladoceran, *Simocephalus serrulatus*	S	U	Aldrin	48	32	27	Sanders & Cope, 1966
Isopod, *Asellus breicaudus*	S	U	Aldrin	96	8	7	Sanders, 1972
Scud, *Gammarus fasciatus*	S	U	Aldrin	96	4,300	3,642	Sanders, 1972
Scud, *Gammarus fasciatus*	S	U	Aldrin	96	5,600	4,743	Sanders, 1972
Scud, *Gammarus lacustris*	S	U	Aldrin	96	38,500	32,609	Gaufin, et al. 1965
Scud, *Gammarus lacustris*	S	U	Aldrin	96	9,800	8,301	Sanders, 1969
Glass shrimp, *Palaemonetes kadiakensis*	S	U	Aldrin	96	50	42	Sanders, 1972

Table 2. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (µg/l)	Adjusted LC50 (µg/l)	Reference
Mayfly, *Ephemerella grandis*	S	U	Aldrin	96	9	8	Gaufin, et al. 1965
Stonefly, *Acroneuria pacifica*	S	U	Aldrin	96	143	121	Jensen & Gaufin, 1964
Stonefly, *Pteronarcys californica*	S	U	93% aldrin	96	180	152	Jensen & Gaufin, 1964
Stonefly, *Pteronarcys californica*	S	U	Technical grade aldrin	96	1.3	1.1	Sanders & Cope, 1968

* S = static

** U = unmeasured

Geometric mean of adjusted values: Dieldrin = 26 µg/l $\frac{26}{21} = 1.2$ µg/l

Aldrin = 80 µg/l $\frac{80}{21} = 3.8$ µg/l

Table 3. Freshwater fish chronic values for aldrin/dieldrin

Organism	Test*	Limits (ug/l)	Chronic Value (ug/l)	Reference
Steelhead trout, *Salmo gairdneri*	E-L	0.12-0.39	0.11**	Chadwick & Shumway, 1969
Guppy, *Poecilia reticulata*	LC	0.2-1.0	0.4**	Roelofs, 1971

*E-L = embryo-larval, LC = life cycle or partial life cycle

**All chronic data are for dieldrin

Geometric mean of chronic values = 0.21 µg/l $\frac{0.21}{6.7}$ = 0.031 µg/l

Lowest chronic value = 0.11 µg/l

Table 4. Freshwater plant effects for aldrin/dieldrin

Organism	Effect	Concentration (µg/l)	Reference
Alga, *Scenedesmus quadricaudata*	22% reduction in biomass in 10 days	100 (dieldrin)	Stadnyk & Campbell, 1971
Diatom, *Navicula seminulum*	50% reduction in growth in 5 days	12,800 (dieldrin)	Cairns, 1968
Water meal, *Wolffia papulifera*	Reduced population growth in 12 days	10,000 (dieldrin)	Worthley & Schott, 1971
Water meal, *Wolffia papulifera*	Reduced population growth in 12 days	10,000 (aldrin)	Worthley & Schott, 1971

Lowest plant value for dieldrin = 100 µg/l

Lowest plant value for aldrin = 10,000 µg/l

Table 5. Freshwater residues for aldrin/dieldrin

Organism	Bioconcentration Factor*	Time (days)	Reference
Alga, *Scenedesmus obliquus*	128	2.5	Reinert, 1972
Community dominated by the alga, *Tribonema minus*	5,558	4-6 wks	Rose & McIntire, 1970
Community of alga and diatoms including *Stigeoclonium subsecundum*, *Synedria ulna*, *Epithemia sorex*, *Cocconeis placentula* var. *euglypta*, and *Nitzschia* sp.	3,188	4-6 wks	Rose & McIntire, 1970
Cladoceran, *Daphnia magna*	1,395	3	Reinert, 1972
Freshwater mussel, *Lampsilis siliquoidea*	1,030	7-21	Bedford & Zabik, 1973
Steelhead trout (newly hatched alevin), *Salmo gairdneri*	3,225	35	Chadwick & Shumway, 1969
Lake trout (yearling), *Salvelinus namaycush*	68,286**	152	Reinert, et al. 1974
Channel catfish, *Ictalurus punctatus*	2,385***	70	Shannon, 1977b
Channel catfish, *Ictalurus punctatus*	2,993***	28	Shannon, 1977a
Guppy, *Poecilia reticulata*	9,862	32	Reinert, 1972
Guppy, *Poecilia reticulata*	28,787	160-230	Roelofs, 1971

Maximum Permissible Tissue Concentration

Organism	Action Level or Effect	Concentration (mg/kg)	Reference
Man	Fish and shellfish - smoked, frozen or canned	0.3	FDA Admin. Guideline 7420.08

Table 5. (Continued)

Organism	Action Level or Effect	Concentration (mg/kg)	Reference
Man	Fish and shellfish - raw edible portion	0.3	FDA Admin. Guideline 7420.09
Domestic animals	Animal feed	0.03	FDA Admin. Guideline 7426.04
Rainbow trout, *Salmo gairdneri*	Altered amonia detoxifying mechanism	0.36 of diet	Mehrle & Bloomfield, 1974
Rainbow trout, *Salmo gairdneri*	Altered phenylalanine metabolism	0.36 of diet	Mehrle & DeClue, 1972

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* All bioconcentration factor data are for dieldrin

** May not be at equilibrium

***Data are for dorsal muscle.

Geometric mean bioconcentration factor for all species = 3,238

Geometric mean whole fish bioconcentration factor = 15,482

Lowest residue concentration = 0.03 mg/kg $\frac{0.03}{15,482}$ = 0.0000019 mg/kg or 0.0019 µg/l

Table 6. Other freshwater data for aldrin/dieldrin

Organism	Test Duration	Effect	Result (µg/l)	Reference
		Dieldrin		
Amoeba, Acanthamoeba castellanii	6 days	No effect on survival	10,000	Prescott, et al. 1977
Tubificids (mixture), Tubifex and Limnodrilus	96 hrs	LC50	6,700	Whitten & Goodnight, 1966
Aquatic insects	6 mos	Bioconcentration in naturally exposed animals	4,620	Bulkley, et al. 1974
Stonefly, Pteronarcys californica	30 days	LC50	2	Jensen & Gaufin, 1966
Stonefly, Acroneuria pacifica	30 days	LC50	0.2	Jensen & Gaufin, 1966
Midge, Chironomus tentans	24 hrs	LC50	0.9	Karnak & Collins, 1974
Rainbow trout, Salmo gairdneri	17-23 days	Lethal muscle tissue bioconcentration	3,348	Holden, 1966
Rainbow trout, Salmo gairdneri	140 days	Altered concentrations of 11 amino acids	1 mg/kg/wk	Mehrle, et al. 1971
Rainbow trout, Salmo gairdneri	140 days	Increased lipid control	0.2 mg/kg/wk	Macek, et al. 1970
Rainbow trout, Salmo gairdneri	168 days	Equilibrium bioaccumulation of 1.05 ppm	0.2 mg/kg/wk	Macek, et al. 1970
Carp, Cyprinus carpio	96 hrs	100% mortality of embryos	5,000	Malone & Blaylock, 1970
Channel catfish, Ictalurus punctatus	210 days	Reduced growth	4 µg/g of diet (dry wt.)	Argyle, 1975
Black bullhead, Ictalurus melas	36 hrs	LC50	2.5	Ferguson, et al. 1965

Table 6. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Green sunfish, *Lepomis cyanellus*	111 hrs	Concentration in blood at death	5.65 µg/g	Hogan & Roelofs, 1971
Green sunfish, *Lepomis cyanellus*	111 hrs	Concentration in brain at death	10.31 µg/g	Hogan & Roelofs, 1971
Walleye, *Stizostedion vitreum*	embryonic stage of develop.	Behavioral aberrations of yolk sac fry	12.2	Hair, 1972
Toad (tadpoles), *Bufo woodhousi*	96 hrs	LC50	150	Sanders, 1970
Frog (tadpoles), *Pseudacris triseriata*	96 hrs	LC50	100	Sanders, 1970
		Aldrin		
Amoeba, *Acanthamoeba castellani*	6 days	No effect on survival	10,000	Prescott, et al. 1977
Cladoceran, *Daphnia magna*	3 days	Bioconcentration	14,100	Johnson, et al. 1971
Mayfly, *Hexagenia bilineata*	3 days	Bioconcentration	6,300	Johnson, et al. 1971
Stonefly, *Pteronarcys californica*	30 days	LC50	2.5	Jensen & Gaufin, 1966
Stonefly, *Acroneuria pacifica*	30 days	LC50	22	Jensen & Gaufin, 1966
Midge, *Chironomus* sp.	3 days	Bioconcentration	4,600	Johnson, et al. 1971
Carp, *Cyprinus carpio*	--	Significant increase of sodium in profused gill	180	McBride & Richards, 1971
Black bullhead, *Ictalurus melas*	36 hrs	LC50	12.5	Ferguson, et al. 1965
Bluegill, *Lepomis macrochirus*	--	Aldrin 50% inhibition dose or Na^+-K^+ ATPase	30 µM	Yap, et al. 1975

Table 6. (Continued)

Organism	Test Duration	Effect	Result (µg/l)	Reference
Toad (tadpoles), *Bufo woodhousii*	96 hrs	LC50	150	Sanders, 1970

Lowest dieldrin value = 0.2 µg/l

Lowest aldrin value = 2.5 µg/l

SALTWATER ORGANISMS

Introduction

Aldrin and dieldrin are chlorinated cyclodiene compounds that have in the past, been two of the most widely used insecticides. Aldrin was applied to soils and foliage using soil injection or aerial techniques; since leaching by water was minimal, soil erosion and sediment transport were the two major routes for aldrin to enter aquatic environments. Aldrin and dieldrin are often considered together, because aldrin is rapidly converted to dieldrin by metabolism by plants and animals or by photo- decomposition. Therefore, although aldrin and dieldrin are considered separately for purpose of comparison, dieldrin is of the greater concern in the aquatic environment.

The acute toxicities of aldrin and dieldrin and the persistence and bioaccumulation potential for dieldrin have been studied using estuarine plants and animals. Bioaccumulation by estuarine organisms and/or subsequent transfer to other animals in estuarine food-webs have been documented in field-studies and laboratory experiments. Long-term test results indicate that dieldrin is chronically toxic to estuarine fishes and crabs, although the exact mechanism of toxicity is not known.

Acute Toxicity

All species of saltwater fish tested were sensitive to acute exposures to aldrin (13 species) or dieldrin (16 species) (Table 7). In flow-through exposures, the unadjusted 48- or 96-hour LC50 values for six fishes ranged from 2.0 to 7.2 µg aldrin/l (Butler, 1963; Earnest and Benville, 1972; Korn and Earnest; 1974; and Lowe, data sheets). The unadjusted acute LC50 values for eight fishes exposed to dieldrin differed and ranged from 0.66 to 24.0 µg/l in flow-through tests (Butler, 1963; Earnest and Benville, 1972; Korn and Earnest, 1974; Lowe, data sheets; Parrish, et al. 1973; Schoettger, 1970; and Wade, 1969). Generally, LC50 values for aldrin are slightly higher than those for dieldrin in tests where the same species were tested, but for practical purposes, the acute toxicities for these two chemicals can be considered the same.

Estuarine invertebrate species are acutely sensitive to both aldrin and dieldrin, but there is greater differences in reported LC50 values for these species than for fishes (Table 8). Unadjusted invertebrate LC50 or EC50 values ranged from 0.37 to 33.0 µg aldrin/l and 0.28 to 240.0 µg dieldrin/l. The most sensitive species tested was the commercially important pink shrimp; the 24-hour LC50 value for aldrin was 0.37 µg/l, while the 48-hour LC50 value for dieldrin was 0.28 µg/l (unmeasured), and the 96-hour LC50 value was 0.7 µg/l (measured) in flowing water exposures (Lowe, data sheets; Parrish, et al. 1973). Other crustaceans were less sensitive and their acute LC50 values ranged from 3.0 to 240.0 µg/l (Butler, 1963; Lowe, data sheets; Parrish, et al. 1973; Schoettger, 1970).

Acute toxicity test conditions can affect the results of tests with fishes and invertebrates. For example, LC50 values based on static exposures of aldrin or dieldrin with three fish and two invertebrate species are higher than LC50 values based on flow-through exposures where comparable data are available (Earnest and Benville, 1072; Eisler, 1969, 1970b; Lowe, data sheets; and Parrish, et al. 1973). In addition, LC50 values for dieldrin based on unmeasured concentrations were higher than those based on measured concentrations in tests with sheepshead minnows and two shrimp species (Eisler, 1969; Parrish, et al. 1973). Therefore, if relative sensitivities of species are to be understood, knowledge of test procedures is necessary.

Chronic Toxicity

No entire life-cycle or embryo-larval tests have been reported for aldrin or dieldrin. However, results (Table 11) of long-term exposures of invertebrate species and a fish species to dieldrin in food (Klein and Lincer, 1974) or water (Epifanio, 1971; Lane and Livingston, 1970) indicate a need for such data. The LC50 value of dieldrin to the sailfin molly after 34 weeks of exposure was approximately one-fourth that after 48-hours (Tables 7 and 11). Fiddler crabs (*Uca pugilator*) fed 100 ng dieldrin/g for 15 days (Table 11) demonstrated unusual running behavior (Klein and Lincer, 1974).

Plant Effects

Information on the sensitivity of aquatic plants, including algae and rooted vascular plants, indicates that they are much less sensitive than are fish and invertebrate species. Productivity and growth rates were reduced at concentrations of approximately 950 to 1,000 µg/l in three 4- to 36-hour static tests using one alga and mixed-population communities (Batterton, et al. 1971; Butler, 1963).

Residues

Bioconcentration factors (BCF) for dieldrin (Tables 10 and 11) range from 400 to 8,000 for fish or shellfish (Epifanio, 1973; Lane and Livingston, 1970; Mason and Rowe, 1976; Parrish, 1974;

and Parrish, et al. 1973). Bioconcentration factors for oysters were higher for long exposure periods because dieldrin concentrations in tissues reached steady-state after extended periods (several weeks) of exposure (Mason and Rowe, 1976; Parrish, 1974; Parrish, et al. 1973). Therefore, long exposures are necessary to attain steady-state bioconcentration factors. After 34 weeks of exposure to dieldrin, sailfin mollies exhibited BCF's of 3,867 to 4,867 in muscle; BCF's for liver, brain, gill, intestine, and blood ranged from 10,500 to 50,000 (Lane and Livingston, 1970). Spot exposed to dieldrin for 35 days, depurated the chemical to non-detectable body-burdens within 13 days of holding in dieldrin-free saltwater (Parrish, et al. 1973). Concentrations in edible tissues were slightly less (about 15 percent) than concentrations in whole spot; however, concentrations in liver were two to 13 times that in spot muscle.

Data Interpretation and Use of Guidelines

Acute toxicity of aldrin and dieldrin will be underestimated by static tests and by toxicity tests in which the concentration of aldrin or dieldrin is not measured by chemical analysis. After applying adjustment factors for test conditions, the variability in sensitivity of fishes to aldrin and dieldrin was reduced so they differed by less than a factor of 50 for all species. When the geometric mean of the LC50 value for aldrin is divided by the Guideline's species sensitivity factor of 3.7, a value of 1.4 µg/l results. The Guidelines adjustment factors for test conditions and species sensitivity seem reasonable because none of the geometric mean adjusted LC50 values for any species is lower than the

Final Fish Acute Value of 1.4 µg aldrin/l although some are close. The Guidelines are designed to obtain a Final Acute Value that provides an estimate of an LC50 value that is less than that of 95 percent of all fish species. When the geometric mean of the LC50 value for dieldrin is divided by the Guidelines species sensitivity factor of 3.7, a Final Fish Acute Value of 0.85 µg/l results. This value is lower than the geometric mean adjusted LC50 values for 13 of 16 species tested. Therefore, since the Guidelines are designed to provide a Final Fish Acute Value which is lower than or equal to the LC50 value of 95 percent of the species, the test conditions and sensitivity adjustment factors appear appropriate.

Invertebrate acute values must also be adjusted for test conditions and species sensitivities. When the Final Invertebrate Acute Value is obtained from the geometric mean of the adjusted LC50 values divided by the species sensitivity factor of 49, a Final Invertebrate Acute Value of 0.084 µg aldrin/l results. The adjustment factors seem reasonable because the geometric mean adjusted LC50 values for six of the seven tested species are greater than the Final Invertebrate Acute Value; the adjusted LC50 value of 0.074 µg/l for pink shrimp is only slightly lower.

The geometric mean of the adjusted LC50 values for dieldrin, when divided by the species sensitivity factor of 49, gives a Final Invertebrate Acute Value of 0.16 µg dieldrin/l. The adjustment factors seem reasonable because the geometric mean adjusted LC50 values for seven of the eight tested species are greater than the Final Invertebrate Acute Value; the adjusted LC50 value for one test with pink shrimp was less than the Final Invertebrate Acute Value.

Dieldrin was bioconcentrated in edible portions of fish and shellfish by 2,000 to 8,000 times the concentration in water. The acceptable residue level, 0.03 µg/g for animal feed, divided by the geometric mean bioconcentration factor of 4,367 for whole fish, gives a Residue Limited Toxicant Concentration (RLTC) of 0.0069 µg/l.

CRITERION FORMULATION

Saltwater-Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value = 0.85 μg/l

Final Invertebrate Acute Value = 0.16 μg/l

Final Acute Value = 0.16 μg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = 950 μg/l

Residue Limited Toxicant Concentration = 0.0069 μg/l

Final Chronic Value = 0.0069 μg/l

0.44 x Final Acute Value = 0.070 μg/l

No saltwater criterion can be derived for dieldrin using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

However, results obtained with dieldrin and freshwater organisms indicate how a criterion may be estimated. For freshwater organisms the Final Fish Chronic Value divided by the Final Fish Acute Value is 0.031/1.6 = 0.019. When this value is multiplied times the saltwater Final Fish Acute Value, an estimated Final Fish Chronic Value of 0.85 x 0.019 = 0.016 μg/l is obtained. Therefore, the Final Chronic Value of 0.0069 μg/l, based on the RLTC, should not cause adverse chronic effects on fish or invertebrate species.

To estimate a criterion for dieldrin, the maximum concentration is the Final Acute Value of 0.16 µg/l and the 24-hour average concentration is the Final Chronic Value of 0.0069 µg/l. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For dieldrin the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 0.0069 µg/l as a 24-hour average and the concentration should not exceed 0.16 µg/l at any time.

Table 7. Marine fish acute values for aldrin/dieldrin

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
			Aldrin			
American eel, *Anguilla rostrata*	S	U	96	5.0	2.73	Eisler, 1970b
Mummichog, *Fundulus heteroclitus*	S	U	96	8.0	4.37	Eisler, 1970b
Mummichog, *Fundulus heteroclitus*	S	U	96	4.0	2.19	Eisler, 1970a
Striped killifish, *Fundulus majalis*	S	U	96	17.0	9.29	Eisler, 1970b
Atlantic silverside, *Menidia menidia*	S	U	96	13.0	7.11	Eisler, 1970b
Threespine stickleback, *Gasterosteus aculeatus*	S	U	96	39.8	21.76	Katz, 1961
Threespine stickleback, *Gasterosteus aculeatus*	S	U	96	27.4	14.98	Katz, 1961
Striped bass, *Morone saxatilis*	FT	U	96	7.2	5.54	Korn & Earnest, 1974
Spot, *Leiostomus xanthurus*	FT	U	48	3.2	2.0	Lowe, undated
Shiner perch, *Cymatogaster aggregata*	S	U	96	7.4	4.05	Earnest & Benville, 1972
Shiner perch, *Cymatogaster aggregata*	FT	U	96	2.26	1.74	Earnest & Benville, 1972
Dwarf perch, *Micrometrus minimus*	S	U	96	18.0	9.84	Earnest & Benville, 1972
Dwarf perch, *Micrometrus minimus*	FT	U	96	2.03	1.56	Earnest & Benville, 1972
Bluehead, *Thalassoma bifasciatum*	S	U	96	12.0	6.56	Eisler, 1970b
White mullet, *Mugil curema*	FT	U	48	2.8	1.75	Butler, 1963

Table 7. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Striped mullet, *Mugil cephalus*	S	U	96	100.0	54.67	Eisler, 1970b
Striped mullet, *Mugil cephalus*	FT	U	48	2.0	1.25	Lowe, undated
Northern puffer, *Sphaeroides maculatus*	S	U	96	36.0	19.68	Eisler, 1970b
			Dieldrin			
American eel, *Anguilla rostrata*	S	U	96	0.9	0.49	Eisler, 1970b
Chinook salmon, *Oncorhynchus tshawytscha*	FT	U	96	1.47	1.13	Schoettger, 1970
Sheepshead minnow, *Cyprinodon variegatus*	S	U	48	5.82***	2.58	Wade, 1969
Sheepshead minnow, *Cyprinodon variegatus*	FT	U	48	24.0	15.0	Lowe, undated
Sheepshead minnow, *Cyprinodon variegatus*	FT	M	96	10.0	10.0	Parrish, et al. 1973
Mummichog, *Fundulus heteroclitus*	S	U	96	5.0	2.73	Eisler, 1970a
Mummichog, *Fundulus heteroclitus*	S	U	96	16.0	8.75	Eisler, 1970b
Mummichog, *Fundulus heteroclitus*	S	U	96	5.0	2.73	Eisler, 1970b
Striped killifish, *Fundulus majalis*	S	U	96	4.0	2.19	Eisler, 1970b
Sailfin molly, *Poecilia latipinna*	S	U	48	10.81***	4.79	Wade, 1969
Atlantic silverside, *Menidia menidia*	S	U	96	5.0	2.73	Eisler, 1970b

Table 7. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Threespine stickleback, *Gasterosteus aculeatus*	S	U	96	15.3	8.36	Katz, 1961
Threespine stickleback, *Gasterosteus aculeatus*	S	U	96	13.1	7.16	Katz, 1961
Striped bass, *Morone saxatilis*	FT	U	96	19.7	15.17	Korn & Earnest, 1974
Spot, *Leiostomus xanthurus*	FT	U	24	3.2	1.63	Lowe, undated
Shiner perch, *Cymatogaster aggregata*	S	U	96	3.7	1.53	Earnest & Benville, 1972
Shiner perch, *Cymatogaster aggregata*	FT	U	96	1.5	1.16	Earnest & Benville, 1972
Dwarf perch, *Micrometrus minimus*	S	U	96	5.0	2.73	Earnest & Benville, 1972
Dwarf perch, *Micrometrus minimus*	FT	U	96	2.44	1.88	Earnest & Benville, 1972
Bluehead, *Thalassoma bifasciatum*	S	U	96	6.0	3.28	Eisler, 1970b
White mullet, *Mugil curema*	FT	U	48	7.1	4.43	Butler, 1963
Striped mullet, *Mugil cephalus*	FT	U	48	3.2	2.0	Lowe, undated
Striped mullet, *Mugil cephalus*	FT	U	48	3.2	2.0	Lowe, undated
Striped mullet, *Mugil cephalus*	FT	U	48	0.66	0.41	Lowe, undated
Striped mullet, *Mugil cephalus*	S	U	96	23.0	12.57	Eisler, 1970b

Table 7. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (µg/l)	Adjusted LC50 (µg/l)	Reference
Northern puffer, *Sphaeroides maculatus*	S	U	96	34.0	18.59	Eisler, 1970b

* S = static; FT = flow-through

** M = measured; U = unmeasured

***Geometric mean of 18 means

Geometric mean of adjusted values: aldrin = 5.2 µg/l $\frac{5.2}{3.7} = 1.4$ µg/l

dieldrin = 3.2 µg/l $\frac{3.2}{3.7} = 0.85$ µg/l

Table 8. Marine invertebrate acute values for aldrin/dieldrin

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
			Aldrin			
Eastern oyster, Crassostrea virginica	FT	U	96	25.0***	19.25	Butler, 1963
Sand shrimp, Crangdon septemspinosa	S	U	96	8.0	6.78	Eisler, 1969
Hermit crab, Pagurus longicarpus	S	U	96	33.0	27.95	Eisler, 1969
Grass shrimp, Palaemonetes vulgaris	S	U	96	9.0	7.62	Eisler, 1969
Korean shrimp, Palaemon macrodactylus	S	U	96	0.74	0.63	Schoettger, 1970
Korean shrimp, Palaemon macrodactylus	FT	U	96	3.0	2.3	Schoettger, 1970
Pink shrimp, Penaeus duorarum	FT	U	24	0.37	0.074	Lowe, undated
Blue crab (juvenile), Callinectes sapidus	FT	U	48	23.0	7.62	Lowe, undated
			Dieldrin			
Eastern oyster, Crassostrea virginica	FT	U	96	34.0***	26.2	Butler, 1963
Eastern oyster, Crassostrea virginica	FT	U	24	15.0***	3.0	Lowe, undated
Eastern oyster, Crassostrea virginica	FT	U	24	240.0***	48.0	Lowe, undated
Eastern oyster, Crassostrea virginica	FT	M	96	31.2***	31.2	Parrish, et al. 1973
Sand shrimp, Crangdon septemspinosa	S	U	96	7.0	5.9	Eisler, 1969
Hermit crab, Pagurus longicarpus	S	U	96	18.0	15.2	Eisler, 1969

Table 8. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Grass shrimp, *Palaemonetes vulgaris*	S	U	96	50.0	42.4	Eisler, 1969
Grass shrimp, *Palaemonetes pugio*	FT	M	96	8.64	8.64	Parrish, et al. 1973
Korean shrimp, *Palaemon macrodactylus*	S	U	96	16.9	14.3	Schoettger, 1970
Korean shrimp, *Palaemon macrodactylus*	FT	U	96	6.9	5.3	Schoettger, 1970
Pink shrimp, *Penaeus duorarum*	FT	M	96	0.7	0.7	Parrish, et al. 1973
Pink shrimp, *Penaeus duorarum*	FT	U	48	0.28	0.093	Lowe, undated
Brown shrimp, *Penaeus aztecus*	FT	U	48	3.2	1.06	Lowe, undated
Blue crab (juvenile), *Callinectes sapidus*	FT	U	48	240.0	79.5	Lowe, undated

* S = static; FT = flow-through

** M = measured; U = unmeasured

***EC50 for decreased shell growth

Geometric mean of adjusted values: aldrin = 4.1 µg/l $\frac{4.1}{49}$ = 0.084 µg/l

dieldrin = 7.9 µg/l $\frac{7.9}{49}$ = 0.16 µg/l

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Table 9. Marine plant effects for aldrin/dieldrin

Organism	Effect	Concentration (ug/l)	Reference
Alga, *Agmenellum quadruplicatum*	Reduced growth rate	950*	Batterton, et al. 1971
Phytoplankton community	84.6-84.8% decrease in productivity after 4 hrs	1,000**	Butler, 1963

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* Dieldrin

** Aldrin

Lowest plant value = 950 µg/l

Table 10. Marine residues for aldrin/dieldrin*

Organism	Bioconcentration Factor	TIME (days)	Reference
Eastern oyster, Crassostrea virginica	8,000**	392	Parrish, 1974
Crab, Leptodius floridanus	400***	16	Epifanio, 1973
Sailfin molly, Poecilia latipinna	4,367	238	Lane & Livingston, 1970
Spot, Leiostomus xanthurus	2,300**	35	Parrish, et al. 1973

Maximum Permissible Tissue Concentration

Organism	Action Level or Effect	Concentration (mg/kg)	Reference
Man	Fish and shellfish - smoked, frozen or canned	0.3	FDA Admin. Guideline 7420.08
Man	Fish and shellfish - raw edible portion	0.3	FDA Admin. Guideline 7420.09
Domestic animals	Animal feed	0.03	FDA Admin. Guideline 7426.04

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* All data are for dieldrin

** Edible tissue

*** Converted from dry to wet weight basis

Geometric mean whole fish bioconcentration factor = 4,367

Geometric mean bioconcentration factor for all species (does not include edible portion of fish) = 2,409

Lowest residue concentration = 0.03 mg/kg $\frac{0.03}{4,367}$ = 0.0000069 mg/kg or 0.0069 µg/l

Table 11. Other marine data for aldrin/dieldrin*

Organism	Test Duration	Effect	Result (µg/l)	Reference
Alga, *Skeletonema costatum*	2 hrs	1,588**	-	Rice & Sikka, 1973
Alga, *Tetraselmis chuii*	2 hrs	859**	-	Rice & Sikka, 1973
Alga, *Isochrysis galbana*	2 hrs	824**	-	Rice & Sikka, 1973
Alga, *Olisthodiscus luteus*	2 hrs	490**	-	Rice & Sikka, 1973
Alga, *Cyclotella nana*	2 hrs	481**	-	Rice & Sikka, 1973
Alga, *Amphidinium carteri*	2 hrs	98**	-	Rice & Sikka, 1973
Clam, *Rangia cuneata*	72 hrs	Bioconcentration factor = 1,600	-	Petrocelli, et al. 1973
Eastern oyster, *Crassostrea virginica*	7 days	Bioconcentration factor = 2,070	-	Mason & Rowe, 1976
Eastern oyster, *Crassostrea virginica*	7 days	Bioconcentration factor = 2,880	-	Mason & Rowe, 1976
Brown shrimp, *Crangon crangon*	48 hrs	LC50	>10, <33	Portmann & Wilson, 1971
Shore crab, *Carcinus macnus*	48 hrs	LC50	>10, <33	Portmann & Wilson, 1971
Fiddler crab, *Uca pugilator*	15 days	Dieldrin in food affected running behavior	0.1 µg/g	Klein & Lineer, 1974
Crab larvae, *Leptodius floridanus*	18 days	Bioaccumulated after consuming food with 213 µg/kg	217 µg/g	Epifanio, 1973
Crab larvae, *Leptodius floridanus*	6 days	LC50, approximately = 1 µg/l	-	Epifanio, 1971

Table 11. (Continued)

Organism	Test Duration	Effect	Result (µg/l)	Reference
Blue crab, *Callinectes sapidus*	10 days	Bioaccumulated 4 to 7 times the daily dose in food	-	Petrocelli, et al. 1975
Sailfin molly, *Poecilia latipinna*	34 wks	LC50	>1.5, <3.0	Lane & Livingston, 1970
Winter flounder, *Pseudopleuronectes americanus*	--	1.21 mg/kg in eggs caused 88% reduction in fertilization relative to controls	-	Smith & Cole, 1973

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* All data are for dieldrin

** Correction factor (0.1) for dry weight analysis

ALDRIN/DIELDRIN

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ALDRIN AND DIELDRIN

Mammalian Toxicology and Human Health Effects

Introduction

During the past decade, considerable information has been generated concerning the toxicity and potential carcinogenicity of the two organochlorine pesticides aldrin and dieldrin. These two pesticides are usually considered together since aldrin is readily expoxidized to dieldrin in the environment. Both are acutely toxic to most forms of life including arthropods, mollusks, invertebrates, amiphibians, reptiles, fish, birds, and mammals. Dieldrin is extremely persistent in the environment. By means of bioaccummulation it is concentrated manyfold as it moves up the food chain.

Aldrin and dieldrin are manmade compounds belonging to the group of cyclodiene insecticides. They are a subgroup of the chlorinated cyclic hydrocarbon insecticides which include DDT, BHC, etc. They were manufactured in the United States by Shell Chemical Company until the U.S. EPA prohibited their manufacture in 1974 (39 FR 37246) under the Federal Insecticide, Fungicide and Rodenticide Act. They are currently manufactured by Shell Chemical Company in Holland. Prior to 1974, both insecticides were available in the United States in various formulations for broad-spectrum insect control. They were used for control of soil pests and grasshoppers, protection of vegetables and fruits, and control of disese vectors including locusts and termites

(Int. Agency Res. Cancer, 1974a,b). In 1974, the U.S.EPA restricted the use of aldrin/dieldrin to termite control by direct soil injection and non-food seed and plant treatment.

Early work by Treon and Cleveland in 1955 suggested that aldrin and dieldrin may have tumor-inducing potential, especially in the liver. Since that time, several conflicting reports of the hepatocarcinogenicity in mice, rats, and dogs have appeared in literature. Studies have been carried out mainly by the U.S. Food and Drug Administration, the National Cancer Institute, and by the manufacturer, Shell Chemical Company. There has been much debate over the type and significance of hepatic damage caused by aldrin and dieldrin. In order to ascertain the human risks associated with aldrin and dieldrin, evaluations of the toxic effects of these pesticides have been carried out on workers in the Shell Chemical Company. The evaluations include epidemiological studies in addition to the more routine toxicity studies. However, it is felt that the number of workers with high exposures was too small and the time interval too short to determine whether or not aldrin and dieldrin represent a cancer threat to humans.

The objective of this report is to examine published studies so as to utilize the most relevant data to develop a criterion for human risk assessment.

EXPOSURE

Exposure to aldrin and dieldrin is from contaminated waters, food products, and air. Because of its persistence, dieldrin has become widespread in the aquatic environment. It is also spread great distances by wind. Since aldrin and dieldrin are used throughout much of the world beyound the United States, it must be assumed that imported food stuffs, such as meat products, contain residues of these pesticides.

Use of aldrin and dieldrin peaked at 19.3 million lbs. in 1966, and 3.6 million in 1956, respectively (39 FR 37251). The subsequent decline in dieldrin use was due, in part, to increased resistance of boll weevils to chlorinated insecticides (Table 1). The use of dieldrin was preferred to aldrin because it required less application due to its persistance.

TABLE 1

Year	Aldrin (1,000 lbs)	Dieldrin (1,000 lbs)
1950	1,456	0
1951	3,288	185
1952	814	750
1953	1,234	1,135
1954	2,993	1,777
1955	4,372	2,585
1956	6,495	8,635
1957	2,431	2,673
1958	4,971	3,074
1959	5,566	3,008
1960	8,109	2,650
1961	9,26	2,764
1962	10,886	2,990
1963	12,152	2,685
1964	12,693	2,052
1965	14,278	1,814
1966	19,327	1,908
1967	18,092	1,478
1968	13,690	1,332
1969	9,902	1,206
1970	8,909	749
1971	11,615	705
1972	11,868	740
1973 (to July 1).	8,721	432
1973 estimated (to Dec. 31)	(10,000)	(576)
1973	9,900	------
1974 (to July 1)	9,700	------

Domestic sales of aldrin and dieldrin from 1950 through July 1, 1974 (39 FR, 1974).

Ingestion from Water

Aldrin and dieldrin have been applied to vast areas of agricultural land and aquatic areas in the United States and in most parts of the world. These pesticides have therefore found their way into most fresh and marine waters. Unlike DDT, aldrin and deildrin are somewhat more soluble in water (27 and 186 mg/l, respectively) (Park and Bruce, 1968). Gunther, et al. (1968) reported dieldrin to be slightly more soluble at 250 mg/l.

In early studies (Weaver, et al. 1965), dieldrin was found in all major river basins (mean concentration 7.5 ng/l) in the United States and it was found more often than any other pesticide. It was also found in the Mississippi delta (U.S. Dep. Agric. 1966) at 10.0 ng/l while aldrin was found as high as 30 ng/l. Marigold and Schulze (1969) reported aldrin and dieldrin at 40 and 70 ng/l, respectively, in streams in the western United States. Leichtenberg, et al. (1970) found levels of dieldrin and aldrin as high as 114 and 407 ng/l, respectively, in surface waters in the United States.

More recently, dieldrin has been reported to be present in many fresh waters in the United States with mean concentrations ranging from 5 to 395 ng/l in surface water and from 1 to 7 µg/l in drinking water (Epstein, 1976).

In 1975 a survey in the United States of aldrin, dieldrin, DDT, and DDT metabolite levels in raw and drinking water was carried out (U.S.EPA, 1976). Dieldrin was found in 117 of 715 samples analyzed (Table 2). The six samples in the highest range were all taken from the same location, three from raw waters and three from finished waters. Three of these six samples also contained aldrin in concentration of 15 to 18 ng/l.

TABLE 2

Dieldrin Concentrations in Raw and Drinking Water
(U.S. EPA, 1976)

No. of Samples	598	94	13	4	6
ng/l	4	4-10	11-20	21-29	56-110

Harris, et al. (1977) summarized the distribution of various chemicals in drinking water in several cities in the United States. Dieldrin was found in concentrations of 1 ng/l in Seattle, Washington, and Cincinnati, Ohio; 2 ng/l in Miami, Florida, and Ottumwa, Iowa; and as high as 50 ng/l in New Orleans, Louisiana.

It has been estimated (MacKay and Wolkoff, 1973) that unlike many chlorinated hydrocarbons that evaporate rapidly from shallow waters, dieldrin has by far the longest half-life of these compounds in water 1 meter in depth. They calculated that the half-life for aldrin and dieldrin would be 10.1 days and 723 days, respectively, compared to 3.5 days for DDT and 289 days for lindane. This long half-life in water combined with the potential for bioconcentration by aquatic organisms such as micororganisms, phytoplankton, mollusks, and fish further enhances the hazard of these two pesticides (Wurster, 1971).

Ingestion from Food

Although aldrin is readily converted to dieldrin, dieldrin itself is stable and persistent in the environment. Because it is lipophilic, dieldrin accumulates in the food chain (Wurster, 1971). The persistence of aldrin and dieldrin in different soils varies with the type of soil and with movement to other areas by water, wind, etc.(Matsumura and Boush, 1967). Dieldrin has been shown to be one of the most persistent of all the organochlorine pesticides (Nash and Woolson, 1967).

It has been estimated that 99.5 percent of all human beings in the United States have dieldrin residues in their tissues (U.S. EPA, 1971). Although there are other origins of contamination, these residue levels are mainly due to contamination of foods of animal origin (Wurster, 1971). The levels of aldrin/dieldrin in several types of food have been summarized by Edwards (1973), Matsumura (1974), and Manske and Johnson (1975). The overall concentration of dieldrin in the diet in the United States has been calculated to be approximately 43 ng/g of food consumed (Epstein, 1976). Table 3 lists the estimated daily dietary intake for aldrin and dieldrin of a 16-to 19-year-old male (Natl. Acad. Sci., 1975).

A bioconcentration factor (BCF) relates the concentration of a chemical in water to the concentration in aquatic organisms, but BCF's are not available for the edible portions of all four major groups of aquatic organisms consumed in the United States. Since data indicate that the BCF for lipid-soluble

TABLE 3

Daily Dietary intake (mg)

	1965	1966	1967	1968	1969	1970
Aldrin	0.001	0.002	0.001	trace	trace	trace
Dieldrin	0.005	0.007	0.001	0.004	0.005	0.005

compounds is proportional to percent lipids, BCF's can be adjusted to edible portions using data on percent lipids and the amounts of various species consumed by Americans. A recent survey on fish and shellfish consumption in the United States (Cordle, et al. 1978) found that the per capita consumption is 18.7 g/day. From the data on the 19 major species identified in the survey and data on the fat content of the edible portion of these species (Sidwell, et al. 1974), the relative consumption of the four major groups and the weighted average percent lipids for each group can be calculated:

Group	Consumption (Percent)	Weighted Average Percent Lipids
Freshwater fishes	12	4.8
Saltwater fishes	61	2.3
Saltwater molluscs	9	1.2
Saltwater decapods	18	1.2

Using the percentages for consumption and lipids for each of these groups, the weighted average percent lipids is 2.3 for consumed fish and shellfish.

Measured steady-state bioconcentration factors were obtained for dieldrin using five species:

Organisms	BCF	Percent Lipids	Adjusted BCF	Reference
Eastern oyster, *Crassostrea virginica*	8,000	1.5	12,266	Parrish, 1974
Spot, *Leiostomus xanthurus*	2,300	3.1	1,706	Parrish, et al. 1973
Lake trout (yearling), *Salvelinus namaycush*	68,286	14.9	10,540	Reinert, et al. 1974
Channel catfish, *Ictalurus punctatus*	2,385	3.2	1,714	Shannon, 1977b
Channel catfish, *Ictalurus punctatus*	2,993	3.2	2,151	Shannon, 1977a

Each of these measured BCF's was adjusted from the percent lipids of the test species to the 2.3 percent lipids that is the weighted average for consumed fish and shellfish. The geometric mean was obtained for each species, and then for all species. Thus, the mean bioconcentration factor for dieldrin and the edible portion of all aquatic organisms consumed by Americans is calculated to be 4,500.

No useful measured bioconcentration factor can be obtained for aldrin because it is rapidly converted to dieldrin by aquatic organisms. In addition, because aldrin is converted to dielrin in soil, aquatic organisms are rarely exposed to aldrin.

However, the equation "Log BCF = 0.76 Log P - 0.23" can be used (Veith, et al. Manuscript) to estimate the BCF for aquatic organisms that contain about eight percent lipids from the octanol-water partition coefficient (P). Based on an octanol-water partition coefficient of 1,000, a steady-state bioconcentration factor for aldrin would be estimated to be 110. An adjustment factor of 2.3/8.0 = 0.2875 can be used to adjust the estimated BCF from the 8.0 percent lipids on which the equation is based to the 2.3 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average bioconcentration factor for aldrin and the edible portion of all aquatic organisms consumed by Americans would be calculated to be 110 x 0.2875 = 32.

Inhalation

Aldrin and dieldrin enter the air through various mechanisms such as spraying, wind action, water evaporation, and adhesion to particulates. Stanley, et al. (1971) reported levels of aldrin and dieldrin in air samples in nine cities in the United States. One sample of the air in Iowa City, Iowa had detectable levels of aldrin (8.0 ng/m^3), and 50 samples taken in Orlando, Florida had detectable amounts of dieldrin, the largest being 29.7 hg/m^3. Various other studies of the air carried out during the 1960's were summarized by Edwards (1973).

In a study conducted by the U.S. EPA from 1970 to 1972 (Epstein, 1976), dieldrin was found in more than 85 percent of the air samples tested. The mean levels ranged from 1 to 2.8 ng/m3. From these levels, the average daily intake of dieldrin by respiration was calculated to be 0.035 to 0.098 µg.

Although aldrin/dieldrin are no longer used in the United States, there is still the possibility of air borne contamination from other parts of the world. Edwards (1973) showed that dieldrin has been transported long distances in the air. Exposure due to inhalation of aldrin and dieldrin from the application of these pesticides was, of course, much greater before the restriction of their use. Pesticide applicators and indiviudals living near agricultural areas were exposed to aldrin/dieldrin through inhalation.

In a recent report, Domanski, et al. (1977) reported no increase in dieldrin concentration in adipose tissue of cigarette smokers as compared to non-smokers although tobacco has high residues of pesticides and is stored many years before use.

Dermal

Dermal exposure to aldrin or dieldrin is limited to those involved in manufacturing or application of these pesticides. Wolfe, et al. (1972) reported that exposure to workers, both manufacturers and applicators, was mainly through dermal absorption rather than from inhalation. Due to the ban on manufaturing of the pesticides in the United States, the possibilities of dermal exposure have been greatly reduce.

PHARMACOKINETICS

Absorption

Heath and Vandekar (1964), using ^{36}Cl-dieldrin (4 percent in arachis oil) showed that absorption by the upper part of the gastroinestinal tract begins almost immediately after oral administration in rats and that the absorption varies with the solvent used. Barnes and Heath (1964) demonstrated that the LD50 varies with the dieldrin-to-solvent ratio. Heath and Vandekar (1964) also demonstrated that absorption is by the poartal vein and not the thoracic lymph duct.

Initially, dieldrin is widespread but within a few hours it is redistributed in favor of the fat. They also stated that following oral treatment at 25 mg/kg, ^{36}Cl-dieldrin could be recovered from the stomach, small intestine, large intestine, and feces after 1 hour.

Distribution

It is well known that dieldrin has a low solubility in water and a high solubility in fat. At 1 and 2 hours after treatment, Heath and Vandekar (1964) detected the highest concentration of ^{36}Cl-dieldrin in fat tissue. They also reported high concentrations in the liver and kidney with moderate concentrations in the brain at these times.

Deichmann, et al.(1968) studied the retention of dieldrin in blood, liver, and fat. Female Osborne-Mendel rats were fed a diet containing 50 mg/kg dieldrin (87 percent purity). The rats were killed on various days of feeding up to 183 days. The concentration of dieldrin in the blood and liver increased for nine days and then leveled off until the end of the six-month period. The concentration of dieldrin in the fat took approximately 16 days to reach a level that was maintained throughout the experiment. The fat had the highest concentrations of dieldrin followed by the liver. The mean concentration in the fat was 474 times that in the blood, while the concentration in the liver was approximately 29 times the blood concentration.

Walker, et al. (1969) studied the distribution of dieldrin in rats and dogs over a two-year period. Dieldrin (99 percent purity) was incorporated into the diet of CFE male and female rats at 0.1, 1.0, and 10 mg/kg and was fed to dogs in gelatin capsules at concentrations equivalent to 0.1 and 1.0 mg/kg of their daily dietary intake. The authors measured the dieldrin residues in whole blood, fat, liver, and brain and found significantly increased concentrations in all tissues compared to those in the controls (Table 4).

TABLE 4

Mean Geometric Dieldrin Concentration (mg/kg) in Rats
104 weeks

	Dietary Level (mg/kg)	Blood	Fat	Liver	Brain
Males	0	0.0009	0.0598	0.0059	0.0020
	0.1	0.0021	0.02594	0.0159	0.0069
	1.0	0.0312	1.493	0.01552	0.1040
	10.0	0.1472	19.72	1.476	0.4319
Females	0	0.0015	0.3112	0.0112	0.0077
	0.1	0.0065	0.8974	0.0348	0.0224
	1.0	0.0861	13.90	0.4295	0.2891
	10.0	0.3954	57.81	2.965	1.130

(Walker, et al. 1969)

The concentrations in the tissues increased with an increase in the dietary concentrations, and the concentrations in the female rats were considerably higher than those in the males. The dieldrin concentrations reached a plateau by the end of the 6th month and remained fairly constant for the remaining 18 months.

In dogs, the blood concentrations increased in both treatment groups of the first 12 weeks. With the higher dose (1.0 mg/kg/diet) the concentration leveled off between 18 and 30 weeks of treatment. However, with the lower dose (0.1 mg/kg/diet) the plateau was reached between 12 and

18 weeks. In the group receiving 1.0 mg/kg/diet the dieldrin concentration in the blood increased significantly during the final 6 weeks of exposure. The dieldrin concentrations in the liver and brain were also dose-related but, as opposed to the results from the rats, showed no significant sex differences. As in other studies, the concentration in the fat was much greater than that in the liver, which in turn, was greater than in the brain.

Additional studies on the distribution of dieldrin were carried out by Robinson, et al. (1969). In this study Carworth rats were fed dieldrin (99+ percent purity) at 10 mg/kg in their diet for 8 weeks. At the end of this time, they were returned to a dieldrin-free diet and killed randomly in pairs up to 12 weeks after withdrawal of the dieldrin diet. The fatty tissue clearly had the highest concentration of dieldrin followed by the liver, brain, and blood. Concentrations of dieldrin in fat returned to control levels after 12 weeks and the decline in dieldrin concentrations was approximately exponential in nature.

Matthews, et al. (1971) investigated the distribution of dieldrin and some of its metabolites in several organs and tissues of both male and female Charles River rats. Three animals of each sex were fasted for eight hours and then given 3 g of food containing 10 mg/kg ^{14}C-dieldrin (96 percent purity). The animals were killed after nine days and dieldrin and metabolic product concentrations were determined. In general, the amount of radioactivity per gram was higher for the female rats. The kidneys and stomachs of the males contained more radioactivity than those of the females. Levels in the lungs and intestines showed similar differences. The other organs and tissues of the females had three to four times the radioactivity of the males. In the females, storage was predominantly as dieldrin, but in males other metabolites, identified as keto dieldrin, and trans-dihydro-aldrin, and a polar metabolite were detected in various tissues.

Hayes (1974) determined the concentration of dieldrin in the fat, liver, kidney, brain, muscle, and plasma following a single oral dose in rats. Male Sprague-Dawley rats were given 10 mg/kg dieldrin (86 percent purity) by stomach tube. The animals were killed at various intervals up to 240 hours and the dieldrin concentration in the tissues was determined. The concentrations in the brain at 4 and 16 hours were 1.5 and 1.0 µg/g, respectively. Hayes assigned a value of one to the concentrations in the brain and calculated the ratio of the concentrations in other tissues to the concentrations in the brain at 4 and 16 hours (Table 5).

TABLE 5

Hr.	Brain	Muscle	Liver	Kidney	Plasma	Fat
4	1.00+0	0.62+0.05	2.30+0.11	1.55+0.22	0.20+0.02	7.20+1.1
16	1.00±0	0.55±0.06	3.17±0.25	2.02±0.56	1.35±1.11	17.96±3.2

The concentrations in the tissues remained relatively constant for 24 hours and began to decline at 48 hours. No further samples were taken until 240 hours when all the dieldrin concentrations were below 0.2 μg/g except the concentration in the fat which was 5 μg/g.

In a study done in 1963 on 30 individuals from three different states, the concentrations of chlorinated hydrocarbon pesticides in body fat were determined (Dale and Quinby, 1963). Twenty-eight individuals were from the general population while one had previous DDT exposure and one had aldrin exposure. The mean (±SE) for the general population was 0.15±0.02 μg/g dieldrin while the aldrin exposure was 0.36 μg/g dieldrin (see discussion on aldrin metabolism to dieldrin in the Metabolism section of this report).

In a study of aldrin and dieldrin concentrations in 71 workers involved in pesticide manufacturing, Hayes and Curley (1968) measured the plasma, fat, and urine concentrations by gas-liquid chromatography. Their findings were in accordance with the earlier animal studies. The fat contained the highest concentration of the pesticides followed by the urine and plasma. The mean concentrations of dieldrin in the fat, urine, and plasma of the pesticide workers were 5.67±1.11, 0.242+0.0063, and 0.0185±0.0019 mg/g respectively. These were significantly different from those reported for the general population. The authors reported a high correlation between total hours or intensity of exposure and concentration of dieldrin. However, no correlation could be found between dieldrin concentrations and amount of sick leave.

Another study (Hunter, et al. 1969) involving adult males ingesting 10, 50, or 211 µg dieldrin per day for 18 or 24 months again found a relationship between the dose and the length of exposure and concentration of dieldrin in the fat and blood. In general, the concentration of dieldrin in the samples increased during the first 18 months and either leveled off or rose slightly during the remaining time. The control and 10 µg groups, both of which were given 211 µg/day for the final 6 months, demonstrated a rise in concentrations similar to the rise demonstrated by those who were given 211 µg/day initially. The authors stated that there was no effect on the general health of the individuals receiving the dieldrin for the two-year test.

In the above-mentioned studies, blood concentrations of aldrin or dieldrin were determined using whole blood (Deichmann, et al. 1968; Robinson, et al. 1969; Hunter, et al. 1969; Walker, et al. 1969), or plasma (Hayes and Curley, 1968). Mick, et al. (1971) measured the aldrin and dieldrin concentrations in erythrocytes, plasma, and the alpha-and beta-lipoprotein fractions of the blood of six aldrin workers after the workers had formulated 2 million-pounds of aldrin over a five-week period. The six workers were exposed to aldrin by both inhalation and dermal contact. The blood samples were collected at the conclusion of the five-week exposure and blood plasma concentrations as high as 312 ng/l were measured. No immediate health problems were reported during this time. In all cases, dieldrin concentrations were higher than the aldrin concentrations due to the epoxidation of aldrin to dieldrin. The dieldrin residue in the plasma averaged approximately four times higher than that in the erythrocytes. As the dieldrin residue in the blood increased, the amount in the plasma became proportionally higher. In addition, the beta-lipoprotein fraction usually contained more dieldrin than the alpha fraction.

The work of Mick, et al. (1971) was confirmed in part by Skalsky and Guthrie (1978). Using labelled pesticides of 98 percent purity incubated with various fractions of human blood _in vitro_ Skalsky and Guthrie were able to demonstrate that dieldrin and DDT bind to albumin and beta-lipoprotein.

Metabolism

Aldrin and its epoxidation product, dieldrin, are both cyclopentadiene insecticides. Since epoxidation of aldrin to dieldrin was first reported by Radomski and Davidow in 1953, there have been many reports in the literature of the ability of various organisms (i.e., soil microorganisms, plants, fish, and animals, including man) to epoxidize this type of double bond. Winteringham and Barnes (1955) first reported this reaction with aldrin in mice. Wong and Terriere (1965) were able to demonstrate the _in vitro_ conversion of aldrin to its epoxide, dieldrin, using microsomes* from male and female rats. The reaction was NADPH-dependent and the enzymes were heat-labile. Winteringham and Barnes also showed that males converted alrdin to dieldrin at a higher rate. No other metabolic products were detected, although the authors noted that polar products could have been overlooked by the methods used. Nakatsugawa, et al. (1965) confirmed the work of Wong and Terriere using microsomes from male rats and rabbits. They also demonstrated a requirement for NADPH and stated that dieldrin was not further metabolized by the microsomes. They reported that lung homogenate was only one-tenth as active as liver in epoxidase activity and that no activity was detected in the kidney, spleen, pancreas, heart, or brain.

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*In this document microsomes refers to the cell-free homogenized liver (including soluble enzymes and microsomes) and not to purified microsomes.

Korte (1963) identified one of the metabolic products of aldrin as aldrin diol in studies with rabbits. Heath and Vandekar (1964) reported the existence of a somewhat polar metabolite which is excreted in the feces. They stated that the feces are the main route of excretion and that little dieldrin is excreted unchanged. They were able to detect other polar metabolites in both urine and feces.

Ludwig, et al. (1964) fed ^{14}C-aldrin to male rats at 4.3 µg/day for three months. The compounds excreted into the urine consisted of aldrin, dieldrin, and unidentified hydrophilic metabolic products. These unidentified products made up 75 percent of the dose excreted in the feces and 95 percent excreted in the urine. Two different products were found in the feces and two in the urine. Two of these four products appeared to be identical by paper and thin-layer chromatography.

Korte and Arent (1965) isolated six urinary metabolites from rabbits treated orally with ^{14}C-dieldrin for 21 weeks. The major metabolite (86 percent) was one of the two enantiomorphic isomers of 6,7 trans-dihydroxy-dihydro-alrdin.

Richardson, et al. (1968) were able to identify two metabolites in urine and feces from male CF rats fed a diet containing 100 mg/kg dieldrin for seven months. Metabolites were isolated from the urine and feces collected during the last month. They determined that the urinary metabolite had a keto group on the number 12 carbon and the epoxide was unchanged. The fecal metabolite was a mono-hydroxyderivative of dieldrin at either the 4a or 4 position. A similar study was carried out (Matthews and Matsumura, 1969) in which male rats were fed a diet of 20 mg/kg purified dieldrin for one month, with the dosage increased to 100 mg/kg for 18 days while the urine and feces were collected. Two metabolites were isolated from the feces and two from the urine. The major fecal metabolite was similar to the mono-hydroxy-derivative isolated by Richardson, et al. (1968) in the feces. The major urinary metabolite was identical to the ketone compound identified by Richardson, et al. in the urine. The minor urinary and fecal metabolites were identical and similar to the 6,7 trans-dihydroxy-dihydro-aldrin described by Korte and Arent (1965).

Matthews and Matsumura (1969) also conducted _in vitro_ experiments using ^{14}C-dieldrin incubated with rat liver microsomes and various co-factors. Thin-layer chromatography of the water-soluble components producted six metabolites in addition to the unchanged dieldrin. Analysis of the water-soluble metabolites revealed a glucoronide conjugate which accounted for approximately 45 percent of the radioactivity. Comparsion of the $R_F$values for the _in vivo_ and _in vitro_ studies showed that the minor urinary/fecal metabolite (i.e., the 6, 7 trans-dihydroxy-dihydro-aldrin) was produced _in vitro_ and that the metabolite freed from the glucoronic acid was also present in the _in vitro_ system in the unconjugated form.

The products identified by Richardson, et al. (1968) and Matthews and Matsumura (1969) represent an oxidized form of dieldrin in the urine and an oxidated, dechlorinated metabolite in the feces which had lost the intact dieldrin ring system.

Hedde, et al. (1970) were able to isolate six metabolic products in the urine of sheep dosed with ^{14}C-dieldrin. Three castrated sheep were given unlabelled dieldrin orally at 2 mg/kg for five days before dosing with ^{14}C-dieldrin. Four other sheep were fed a single oral dose of labelled dieldrin at 20 mg/kg. Urine and feces were collected up to six days after treatment with the labelled dieldrin. Although other determinations were made, only the urine was analyzed quantitatively. After hexane extraction of pH 1 followed by other clean-up procedures, the four hexane-soluble metabolites were separated on Sephadex LH-20 gel. The LH-20 was again used to separate the two water soluble metabolites after they were purified by several procedures, including paper chromatography. The authors postulated that these water-soluble metabolites were a glucoronic acid conjugate of the transdiol and an unidentified conjugate of glucoronic acid and, possibly, glycine.

Feil, et al (1970) were able to identify two to the hexane-soluble metabolites found by Hedde, et al. (1970) in sheep urine. One was the 6,7-trans-dihydroxy-dihydro-aldrin described by Richardson, et al (1968) and the other was the 9-,momo-hydroxy-derivative. Further work on the metabolism of dieldrin (Matthews, et al. (1971) is discussed in the Distribution section of this report where details of treatment are given. Matthews, et al. documented the production of several metabolites of dieldrin including the 6,7-trans-dihydroxy-dihydro-aldrin and a second unidentified polar metabolite excreted in the feces. The mono-hydroxy-lated compound represented the greatest percentage of the radioactivity extracted from the feces of both male and female rats. In male rats, the chloroform extract of the urine consisted of the keto-metabolite described by Klein, et al. (1968). Also, initially, trans-dihydroxy-dihydro-aldrin was found in the urine of the male rats along with unchanged dieldrin. Most of the radioactivity extracted from the urine of the female rats was in the form of the trans-dihydroxy-dihydro-aldrin, and initially contained up to 20 percent dieldrin.

The metabolism and excretion of dieldrin appears to be more rapaid in male than in female rats. Investigators attribute this to the males' ability to produce the more polar metabolites, especially the keto-product which is excreted into the urine.

A recent paper has appeared on the comparative metabolism of dieldrin in rodents. Baldwin, et al. (1972) treated a male CFE rat with 3 mg/kg of ^{14}C-labelled dieldrin and two male CF1 mice with 10 mg/kg. The urine and feces were collected for the following seven or eight days. The authors reported that the CFE rat excreted the pentachloroketone derivative in the urine but that the CF1 mice did not. Conversely, the mice produced an unidentified urinary metabolite which the rat did not. The 6,7-trans-dihydorxy-dihydroaldrin was found in the feces of the mice and the rat, and a dicarboxylic derivative was found in the urine of all three animals.

A review of the literature on the metabolism of dieldrin and endrin in rodents has been compiled by Bedford and Hutson (1976). They summarized the four known metabolic products of dieldrin as they 6,7-trans-dihydroxy-dihydroaldrin (trans-diol) and the tri-cyclic dicarboxylic acid (both of which are products of the trans-formation of the epoxy group), the syn-12-hydroxy-dieldrin (a mono-hydroderivative), and the pentachloroketone.

In comparing dieldrin metabolism in acute of short-term studies versus chronic, low-dose exposure, it must be mentioned that organochlorine compounds, including dieldrin, have been shown to induce the mixed function oxidases (MFO) found in the liver (Kohli, et al. 1977). It is therefore possibel, in the long-term animal studies, that investigators have been observing the results of high levels of these enzymes and that the percentages and amounts of certain metabolites may be misleading. Baldwin, et al. (1971) in a limited study, were able to show some inducability in the CFE male rat but not in the CF1 male mouse. They induced the enzymes by prefeeding the animals for 21 days with low doses (i.e., 10 or 25 mg/kg in diet) of dieldrin. If the results of the Kohli, et al. study are to be accepted, then one may assume that since man is subject to chronic, low-dose exposure to many MFO inducers (including various organochlorine pesticides), this exposure may affect studies of dieldrin metabolism.

Excretion

As mentioned in the Distribution and Metabolism sections of this report, aldrin and/or dieldrin are excreted mainly in the feces and to some extent in the urine in the form of several metabolites that are more polar than the parent compounds. Usually, a plateau is reached in most tissues when the dose is held relatively constant. However, if the dosage increases, the body concentrations will increase and vice versa.

The early work of Ludwig, et al. (1964) demonstrated that male Wistar rats administered daily with low doses of ^{14}C-labelled aldrin (4.3 μg for 12 weeks) excreted approximately nine times as much of the radioactivity in the feces as in the urine. After about two weeks of treatment, the rats were excreting 80 percent of the daily dose of aldrin and this increased to 100 percent after eight weeks. Twenty-four hours after the final dose (12 weeks), the animals had excreted 88 percent of the total radioactivity fed. This increased to 98 percent after six weeks and greater than 99 percent after 12 weeks. It appears that after eight weeks of feeding aldrin, a saturation level was attained which did not increase with continued feeding at the same concentration. The concentrations in the body decreased rapidly once the feeding was terminated.

In a study with rabbits administered ^{14}C-deildrin orally over a 21-week period (total dose 56 to 58 mg/kg), Korte and Arent (1965) reported somewhat conflicting results. At the end of the feeding (22nd week) 42 percent of the total radioactivity had been excreted with two to three times as much in the urine as in the feces. The level in the feces was negligible after 24 weeks while the amount in the urine was up to 43 percent at 52 weeks.

It must be kept in mind that aldrin is metabolized to dieldrin which is then converted to more polar metabolites for excretion. It is possible that the increased amount of radioactivity noted by Korte and Arent in the feces after treatment with aldrin could be due to the less polar aldrin or deldrin as compared to the more polar metabolites excreted in the urine or to a basic in metabolism of deildrin in the rabbit.

The work of Robinson, et al. (1969) on the metabolism of dieldrin has been summarized in the Metabolism section of this report. These investigators also studied the loss of dieldrin (99+ percent purity) from the liver, blood, brain, and adipose tissue of male CFE rats fed 10 mg/kg in their diet for eight weeks. Figure 1 illustrates the loss of dieldrin from these tissues. During the period of observation, approximately 99 percent of the dieldrin was excreted at various rates from the tissues. However, it must be noted that the analysis was performed by gas-liquid chromatography and that later investigators (Matthews, et al. 1971) have found liver can contain approximately 30 percent of products other than dieldrin, a fact which may have been overlooked by Robinson, et al. The fat and brain contained greater than 99 percent dieldrin and the excretion times correspond to those for the rat observed by Korte and Arent, in their work six years earlier.

It can be seen from Figure 1 that three of the four slopes for dieldrin loss were not linear and that with the blood and liver, loss was rapid at first and then slowed down. Estimates for the half-life of dieldrin in the liver and blood were 1.3 days for the period of rapid elimination and 10.2 days for the slower period. The estimated half-life for dieldrin was 10.3 days in the adipose tissue and 3.0 days in the brain.

In the study of ^{14}C-dieldrin metabolism in sheep (Hedde, et al. 1970) mentioned in the Metabolism section of this report, the excretion of dieldrin or its metabolites was

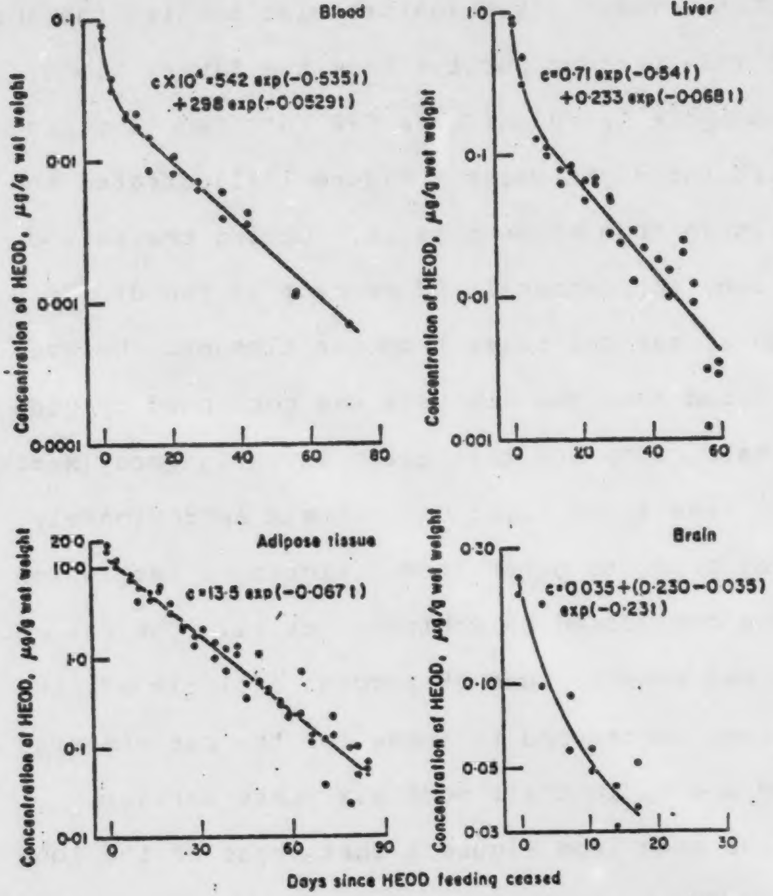

Figure 1

The loss of dieldrin (HOED) from the liver, blood, brain, and adipose tissue of male rats (Robinson, et al. 1969).

higher in the feces than in the urine. This ratio varied considerable due partially to the different doses used. The authors noted that in two very fat sheep the ratio of labelled dieldrin in feces to urine was greater than 10 to 1 but in two thin sheep receiving the same dose, it was slightly greater than 1 to 1. The amount of radioactivity that was exhaled as $^{14}CO_2$ was only 0.25 percent of the total dose. This indicates that virtually none of the dieldrin is broken down to CO_2. With the sheep, less than 50 percent of the total radioactivity was recovered after the five or six days of collection.

Several investigators have shown that removal of dieldrin from the diet results in rapid loss of dieldrin or metabolites from the body, especially the adipose tissue. Barron and Walton (1971) further studied the loss of dieldrin from the body of the rat and also looked at the role of dieldrin in the diet with respect to loss from the adipose tissue. For this study, male Osborne-Mendel rats were fed a diet containing 25 mg/kg dieldrin (99+ percent purity) for 8 weeks. They were then placed on a normal diet and given four daily, oral doses of ^{14}C-dieldrin equivalent to 25 mg/kg in their diet. After these four days, one-half of the animals were then returned to the dieldrin diet (25 mg/kg) while the rest remained on the normal diet.Groups of five animals were sacrificed on the four days when they received the labelled-dieldrin and on days 7, 9, 11, 16, and 23 after the conclusion of the eight-week feeding. The concentration of dieldrin found in the adipose tissue from the rats receiving the dieldrin diet was approximately

50 µg/g and remained at this level throughout the 23 days following the feeding period. The concentrations in the rats on the normal diet decreased to 4 µg/g at day 23. The authors reported that the half-life of dieldrin in the adipose tissue was about 4.5 days, which is somewhat lower than the 10.3 days calculated by Robinson, et al. (1969) with rats fed only 10 mg/kg dieldrin.

Cole, et al. (1970) measured the appearance of ^{14}C-dieldrin and ^{14}C-endrin in the urine and feces of male Holtzman rats for seven days after a single intravenous dose of 0.25 mg/kg of either chemical. They reported that greater than 90 percent of the radioactivity occured in the feces. Approximately 80 percent of the total dose of labelled dieldrin was excreted in the feces after the seven days, compared with approximately 100 percent for the endrin. Cole, et al. (1970) conducted a similar experiment during a four-day period using bile-fistula rats. They also reported that these rats produced patterns of excretion similar to those observed in the first experiment.

In a comparison of the excretion of dieldrin in the CF1 mouse and CFE rat, Baldwin, et al. (1972) found that after seven or eight days the amount of labelled dieldrin excreted was similar to both species. Also, the feces contained approximately two times as much radioactivity as the urine, and 50 to 70 percent of the total activity was excreted during the collection period. As mentioned in the Metabolism section of this report, the proportion of metabolites varied between the mouse and the rat.

Although there has been extensive work done on the metabolism and excretion of dieldrin in animals, there is understandably less known about the fate of dieldrin in humans. Early work by Cueto and Hayes (1962) demonstrated that dieldrin and some of its metabolites could be detected in the urine of occupationally exposed workers. A later report by Cueto and Biros (1967) compared the levels of dieldrin and other chlorinated insecticides in the urine of 5 men and 5 women in the general population to that of 14 men with different degrees of occupational exposure. The concentrations of dieldrin found in the urine of men and women in the general population were 0.8 ± 0.2 mg/l, and 1.3 ± 0.1 mg/l, respectively. The concentrations found in male workers with low, medium, and high degrees of exposure were 5.3 mg/l (5), 13.8 mg/l (4), and 51.4 mg/l (5), respectively (numbers in parentheses represent the number of individuals per sample). The degrees of exposure were only expressed as relative and no data on the exposures were given.

Hayes and Curley (1968) measured the plasma, fat, and urine concentration of various chlorinated pesticides in workers with occupational exposure to these chemicals. In 14 urine samples, aldrin was present at less than 0.2 mg/l and dieldrin was present at 1.3 to 66.0 mg/l. This is compared to the mean for dieldrin in the general population of 0.8 ± 0.2 mg/l determined in the same laboratory by Cueto and Biros (1967).

A study by Hunter, et al. (1969) concluded that dieldrin had a relatively long half-life in humans. This compares with a half-life of less than ten days reported in animal studies. In the Hunter, et al. study, 12 human volunteers ingested various doses of dieldrin for up to 24 months. The blood and adipose concentrations were determined over this time and the blood levels were followed for eight additional months after termination of the treatment. The authors reported that during this period concentrations of dieldrin in the blood of three of the volunteers did not change significantly. (These concentrations were not given.) In the other nine subjects, the half-life of dieldrin in the blood ranged from 141 to 592 days with a mean of 369 days. These estimates were made on a limited number of samples.

Jager (1970) reported that DeJonge, in an unpublished report, studied the half-life of dieldrin in the blood of 15 aldrin/dieldrin workers who were transferred to other areas. Prior to transfer, these workers had had high exposures to the pesticides and concentrations of aldrin/dieldrin in their blood had reached equilibrium. Measurements of the dieldrin blood concentrations were taken every six months for three years following the transfer. The mean half-life was 0.73 years (approx. 266 days). This is somewhat in agreement with the estimates of Hunter, et al. (1969) of 369 days based on limited data.

It has been reported by these and other authors (Robinson, et al. 1969; Walker, et al. 1969) that there is a direct relationship between the concentration of dieldrin in the blood and that in adipose and other tissues. It seems likely that the half-life in the blood may reflect the overall half-life in other tissues.

EFFECTS

Acute, Subacute, and Chronic Toxicity

The acute toxicity of aldrin and dieldrin has been extensively summarized by Hodge, et al. (1967) and Jager (1970). In many cases, aldrin and dieldrin are considered similar due to the rapid conversion of aldrin to dieldrin (see Metabolism section). Dieldrin, in turn, is metabolized to a variety of more polar products. In some cases, the toxicity of the metabolites has been compared to the parent compound but this information is rather sparse (Soto and Deichmann, 1967).

After ingestion, aldrin and dieldrin are rapidly absorbed from the gastro-intestinal tract. Following absorption, the pesticides are transported from the liver to different sites in the body. They have been found at various levels in the brain, blood (including erythrocytes), liver, and especially the adipose tissue (Mick, et al. 1971; Walker, et al. 1969). In addition, dieldrin has been shown to cross the placenta to the fetus (Hathaway, et al. 1967). Hunter, et al. (1969) demonstrated that a relationship between intake and storage exists and that a plateau is maintained in the tissues unless the dose changes considerably.

It was shown early that the pesticide-to-solvent ratio affects the LD50 (Barnes and Heath, 1964) and that some variation is caused by the solvent employed (Heath and Vandekar, 1964). There is a pronounced variation in toxicity related to route of administration. Toxicity is highest by the intravenous route, followed by oral, then dermal.

This is most likely due to the high blood and central nervous system concentrations produced from intravenous injection. Oral and dermal toxicity is lower due to lower blood concentrations brought about by resorption and storage in adipose tissue. For most species the acute oral toxic dose is between 20 and 70 mg/kg. This includes the rat, mouse, dog, monkey, sheep, and man (Hodge, et al. 1967).

With both aldrin and dieldrin, toxicity in animals appears to be related to the central nervous system. According to Hodge:

> "...a characteristic pattern has been described of stimulation, hyperexcitability, hyperactivity, incoordination, and exaggerated body movement, ultimately leading to convulsion, depression, and death."

There apparently is a direct correlation between blood concentrations and clinical signs of intoxication. Keane, et al. (1969) reported that in dogs, fed daily doses of dieldrin, the first signs of muscle spasms occurred at 0.38 to 0.50 µg/ml blood and convulsions at 0.74 to 0.84 µg/ml.

The symptoms of intoxication in man are similar to those found in mice, rats, and dogs. Jager (1970) described the symptoms resulting from oral or dermal exposure that occur from 20 minutes to 24 hours as:

> "...headache, dizziness, nausea, general malaise, vomiting, followed later by muscle twitching, myoclonic jerks and even convulsions. Death may result from anoxemia."

Changes in the electroencephalogram (EEG) usually result after insecticide intoxication and generally return to normal after recovery (Hootsman, 1962). The transitory change in the EEG has been challanged by several investigators (see Burchfiel, et al. (1976) for recent summary). Work carried out in Rhesus monkeys (Burchfiel, et al. 1976) using technical grade dieldrin (4 mg/kg, i.v. one time or 1 mg/kg i.m. administeredonce a week for 10 weeks) demonstrated that dieldrin can alter the EEG for up to 1 year.

The acute lethal dose of aldrin in man was reported by Jager (1970) and Hayes (1971) based on the summary of Hodge, et al. (1967) to be 5 g or 70 mg/kg respectively. However, Hodge, et al. only speculated on possible human toxic effects from a 1-year feeding study in monkeys. It is known that persons have recovered from acute oral doses of 26 mg/kg aldrin and 44 mg/kg dieldrin so that the acute lethal human dose must be somewhat higher (Hayes, 1971).

The subacute or chronic toxicity of low doses of aldrin and dieldrin to mice, rats, dogs and, to some extent, monkeys, has been reported in many of the carcinogenicity studies included herein. The resulting effects include shortened life span, increased liver-to-body weight ratio, various changes in liver histology, and induction of hepatic enzymes. Another effect that has been observed is teratogenicity (Ottolenghi, et al. 1974).

Some information is available concerning the subacute or chronic exposure of humans to aldrin and dieldrin. Based on information gained from monitoring workers at the Shell Chemical Company, Jager (1970) reported that 33.2 μg/kg/day can be tolerated by workers for up to 15 years. Above this level some individuals may show signs of intoxication, although others can tolerate two times this level. In another study involving 12 volunteers who ingested dieldrin for up to two years, 3.1 µg/kg/day was tolerated and produced no increase in plasma alkaline phosphatase activity (Hunter, et al. 1969).

Synergism and/or Antagonism

Since aldrin and dieldrin are metabolized by way of the mixed function oxidases (MFO), it must be assumed that any inducer or inhibitor of these enzymes will affect the metabolism of aldrin or dieldrin. Dieldrin and other organochlorine pesticides have been reported to induce the MFO (Kohli, et al. 1977). Baldwin, et al. (1972) reported that prefeeding low doses of dieldrin to rats altered the metabolic products produced after acute dosing. Several reports have appeared on the combined effect of aldrin or dieldrin on the storage of DDT in tissues (Street, 1964; Street and Blau, 1966; and Deichmann, et al. 1969).

In the Deichmann, et al. (1969) study, when aldrin was given along with DDT or after a plateau had been reached in the blood and fat by chronic DDT feeding, the retention of DDT by the blood and fat increased considerably. The authors suggest that this increase in tissue dieldrin concentrations is due to a reduced rate of excretion of DDT.

Walker, et al. (1972) fed groups of mice 50 or 100 mg/kg/diet DDT or a mixture of 5 mg/kg/diet dieldrin and 50 mg/kg/diet DDT for 112 weeks. The highest incidence of tumors was in the dieldrin/DDT group, although it is difficult to determine whether the effect between dieldrin and DDT was additive or synergistic.

Clark and Krieger (1976) studied the metabolism and tissue accumulation of ^{14}C-labelled aldrin (99.3 percent purity) in combination with an inhibitor of oxidative biotransformation (i.e., SKF 525-A). They reported that pretreatment of male Swiss-Webster mice with either 50 or 100 mg/kg SKF 525-A significantly increased the accumulation of radioactivity in the blood, brain, kidney, and liver. The SKF 525-A blocked the epoxidation of aldrin to dieldrin. However, the authors did not feel that differences in metabolite formation or excretion alone could account for the increased accumulation in the tissues.

Teratogenicity

In 1967, Hathaway, et al. established that ^{14}C-dieldrin could cross the placenta in rabbits. Eliason and Posner (1971a,b) demonstrated that ^{14}C-dieldrin crossed the placenta in the rat and that the concentration in the maternal plasma increased as gestation progressed. Deichmann (1972) reported that 25 mg/kg/diet aldrin and dieldrin fed to mice for six generations markedly affected such parameters as fertility, gestation, viability, lactation, and survival of the young, while mice fed lower doses showed fewer or no effects.

In a study by Ottolenghi, et al. (1974) pregnant golden hamsters and pregnant CD-1 mice were given single oral doses of purified aldrin, dieldrin, or endrin at one-half the LD50 (hamsters 50, 30, 5 mg/kg, and mice 25, 15, 2.5 mg/kg, respectively). The hamsters were treated orally on day seven, eight, or nine of gestation and the mice on day nine. All three pesticides caused a significant increase in fetal death in hamsters treated on days seven and eight. Only dieldrin gave significant results on day nine. Hamsters treated on day eight also had the highest number of anomalies (i.e., open eye, webbed foot, cleft palate, and others). These increased anomalies were noted for all three pesticides. The three pesticides also reduced the fetal weight in the hamsters treated on the three different days. No significant difference was observed in the weight or survival of fetuses of treated and control mice; however, a teratogenic effect was observed in mice for all three pesticides. It was less pronounced in the mice than in the hamsters. The author reasoned that the reduced teratogenic effect in mice may be due to the lower doses used in the mice.

Two later studies on the teratogenicity of dieldrin have reached different conclusions. The studies of Chernoff, et al. (1975) and Dix, et al. (1977) both concluded that dieldrin was not teratogenic. Chernoff, et al. tested dieldrin (87 percent purity) and the photo-product, photodieldrin (95 percent purity) in CD-1 mice and CD rats orally at doses lower than those used by Ottolenghi, et al. (1974). The actual doses of dieldrin based on 87 percent purity were 1.3, 2.6, and 5.2 mg/kg/day over a ten-day period (i.e., days 7 to 16 of gestation). The compounds were dissolved in peanut oil. The control animals also received peanut oil. The highest doses of dieldrin produced 41 percent mortality in rats. In mice the highest doses induced significant increases in liver-to-body weight ratios, reduced the weight gain, and produced some fetal toxicity. Photodieldrin at 0.6 mg/kg/day for 10 days also induced a significant increase in the liver-to-body weight ratio in rats but caused no fetal toxicity. However, no teratogenic effects were observed in the mice or rats at any of the doses employed.

Dix, et al. (1977) examined the use of two solvents (corn oil and dimethylsulfoxide (DMSO)) with various doses of dieldrin in CFl mice. The corn oil groups received 1.5 or 4.0 mg/kg/day of 99 percent pure dieldrin orally with suitable controls of corn oil or no treatment. The DMSO groups received 0.25, 0.5, or 1.0 mg/kg/day with similar controls. Both solvent groups were treated on days 6 through 14 of gestation. In the corn oil group, young (7-week) virgin animals were used and the pregnancy rate was very low. With the few animals that survived to term, the only significant effect was delayed ossification in the mice administered the 4 mg dose. The DMSO experiments were conducted with older animals (ten weeks) of proven fertility. These animals demonstrated a significant increase in incidences of delayed ossification and extra ribs. However, the DMSO controls also had a high incidence of these two anomalies. The authors attributed this to the toxic effect of this solvent. DMSO also produced a reduction in maternal and fetal body weights whereas the corn oil did not. No differences were observed in the mean litter size, number of resoprtions, or fetal death with either solvent.

Mutagenicity

Relatively little work has been done on the mutagenicity of aldrin or dieldrin. Of the limited data available, most are concerned with the mutagenicity of dieldrin. This may be sufficient, since aldrin is readily converted to dieldrin in both *in vivo* and *in vitro* systems. Fahrig (1973) summarized the microbial studies carried out up to 1973 on aldrin, dieldrin, and other organochlorine pesticides including DDT and the metabolites of DDT. Aldrin and dieldrin gave negative results with gene conversion in *Saccharomyces cerevisae*, back-mutation in *Serratia marcescens*, forward mutation (Gal R^S) in *Eschericia coli* and forward mutation to streptomycin resistance in *E. coli*. It is important to note that DDT and several of its metabolites also gave negative results in these microbial tests and that no mention of any type of activation system (i.e., mammalian liver enzymes) was made in this summary.

Bidwell, et al. (1975) reported in an abstract that dieldrin was not found to be mutagenic in five strains of *Salmonella typhimurium* with or without the addition of a liver activation system, although the authors did not give dose levels. They also stated that dieldrin was negative in the host-mediated assay, blood and urine analysis, micronucleus test, metaphase analysis, dominant lethal test, and heritable translocation test. The doses used were 0.08, 0.8, and 8.0 mg/kg in corn oil with corn oil used as the control and triethylene melamine (0.5 mg/kg five times) serving as the positive mutagenic control. The pesticide was given orally on a subacute basis.

Three reports on the mutagenicity of aldrin or dieldrin have recently been published. The first examined the mutagenicity of dieldrin and several other pesticides with four strains of _S. typhimurium_ (i.e., TA1535, TA1536, TA1537, and TA1538) with the addition of a rat liver activating system (Marshall, et al. 1976). The second, an in-depth study of nearly 200 pesticides, utilized several microbial indicators and, in some cases, the addition of an activating system (Shirasu, et al. 1977). The third study dealt primarily with strains of _S. typhimurium_ (TA1535, TA100, and TA98) plus a mouse liver activating system (Majumdar, et al. 1977).

In the Marshall, et al. (1976) study, dieldrin was tested at only one concentration, 1000 ug per plate, with and without the addition of phenobarbital-induced rat liver homogenate. In all four strains tested, no increase in mutagenicity was observed at this concentration.

Shirasu, et al. (1977) assayed aldrin with metabolic activation using _E. coli_ B/r WP2 try-hcr$^+$ and WP try-hcr$^-$ and _S. typhimurium_ strains TA1535, TA1537, TA98, and TA100. Dieldrin was assayed without metabolic activation using the _E. coli_ WP2 hcr$^+$, WP2 hcr$^-$ and _S. typhimurium_ TA1535, TA1536, TA1537, and TA1538. According to the authors, both aldrin and dieldrin were considered non-mutagenic in these tests.

Majumdar, et al. (1977), on the other hand, have reported that dieldrin was somewhat mutagenic for _S. typhimurium_ strains TA1535, TA100, and TA98 without metabolic activation and that it was strongly mutagenic for all three strains when liver enzymes from Aroclor-1254*-induced mice were added to the mixtures.

In summarizing the limited microbial mutagenicity studies on aldrin and dieldrin, it must be mentioned that the only reference to any mutagenicity in the Majumdar studies contains several notable inconsistencies. The inconsistencies are: (1) the cultures used were grown for 24 hours rather than the recommended 16 hours; (2) the plates were incubated for 72 hours rather than the conventional 48 hours; and (3) the control values for TA1535 and TA98 were not consistent with those recommended by Ames, et al. (1975).

It is not possible to say that these inconsistencies could account for the positive mutagenic findings but they should be taken into consideration in view of the fact that several other similar, although not identical, studies reported no mutagenic findings with dieldrin. It should be kept in mind that mice apparently metabolize dieldrin differently than do rats (see the Metabolism section of this report). It is possible that the use of the mouse liver enzymes by Majumdar, et al. (1977) may be producing a mutagenic metabolite not seen in other studies.

Studies on the mutagenic effects of dieldrin in organisms other than microorganisms were also somewhat varied. Scholes (1955) reported that dieldrin had no effect on onion root mitosis. However, Markaryan (1966) observed an increase in the cytogenic effects of dieldrin in mouse bone marrow nuclei and Bunch and Low (1973) reported chromosomal aberrations in semi-domestic mallard ducks.

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*Aroclor-1254 is a mixture of PCB's, which induce the MFO in liver (Ames, et al. 1975).

Recently, Majumdar, et al. (1976) studied (1) the effect of dieldrin on chromosomes in mouse bone marrow in vivo and in cultured human WI-38 lung cells, and (2) the cytopathic effect of dieldrin on the cultured human WI-38 cells. They reported a decrease in the mitotic index in both the in vivo mouse bone marrow and in vitro human lung cells with the increasing concentration of dieldrin used. In each test, an increase in chromosome aberrations was observed with the lowest doses employed (1 mg/kg in mouse bone marrow and 1 µg/ml in human cell cultures). The authors also reported a dose- and time-dependent cytotoxic effect on the WI-38 human lung cells.

In addition, Ahmed, et al. (1977) measured unscheduled DNA synthesis (UDS) in SV-40 transformed VA-4 human fibroblasts in vitro with and without an uninduced rat liver activating system using aldrin, dieldrin, DDT, and other pesticides. Both aldrin and dieldrin produced a significant increase in UDS either with or without the activating system at all the doses used.

Carcinogenicity

During the 1960's and the early part of the 1970's, numerous studies on the carcinogenicity of aldrin and dieldrin appeared in literature. These reports include studies on mice, rats, dogs, and monkeys. Of these species, mice appear to be the most susceptible to aldrin/dieldrin. Various strains of both sexes have been examined at different dose levels. The effects range from benign liver tumors to hepatocarcinogenicity with transplantation confirmation to pulmonary metastases. The data on carcinogenicity have been evaluated and discussed extensively, mainly by Epstein (1975a,b, 1976).

Six major studies using various strains of mice have been carried out mainly by long-term feeding at low doses (i.e., 0.1 to 20 mg/kg in the diet). The earliest of these studies was conducted by the U.S. Food and Drug Administration (FDA) (Davis and Fitzhugh, 1962). Using C_3HeB/Fe (C_3H) mice, both males and females were fed either aldrin or dieldrin at 10 mg/kg in the diet for two years. Both aldrin and dieldrin shortened the average life span by two months. The experimental and control group death rate was high, possibly due to overcrowding. Significantly more hepatomas were observed in the treated groups than in the controls for both sexes. In addition, the number of mice with tumors may have been underestimated due to the high mortality which left fewer animals for evaluation.

In an FDA followup study, Davis (1965) examined 100 males and females of the C_3H mice treated with aldrin or dieldrin at the same concentrations as the first study. Again, survival was reduced compared to the control group and there was an increase in benign hyperplasia and benign hepatomas. A re-evaluation of the histological material of both of these studies was carried out by Rueber in 1973 (Epstein, 1975a,b, 1976). He concluded that the hepatomas were malignant and that both aldrin and dieldrin were hepatocarcinogenic for male and female C_3H mice.

In a 1964 abstract, Song and Harville reported some indication of hepatocarcinogenicity in C_3H and CBA mice with aldrin (15 mg/kg) and dieldrin (15 mg/kg) although minimal data are given. Epstein (1975a,b, 1976) reviewed an unpublished study of MacDonald, et al. on technical grade dieldrin in Swiss-Webster mice. The authors concluded that dieldrin was noncarcinogenic but that there was some questions as to the type of lesions.

Walker, et al. (1972) conducted a multi-part study of dieldrin in CFl mice of both sexes. In this study, the dieldrin used was 99+ percent pure and 4-amino-2,3-dimethylazobenzene (ADAB) was used as the positive control. In the first part of the study, diets were prepared containing 0, 0.1, 1.0, and 10 mg/kg dieldrin although 0.01 mg/kg dieldrin was found in the control (0 mg/kg) diet along with low concentrations of other pesticides. The treatment groups were made up of 600, 250, 250, and 400 mice respectively and contained equal numbers of males and females. The ADAB group, which contained 50 mice equally divided as to sex, received 600 mg/kg/diet for six months. Initially, the animals were housed five to a cage, but after the sixth week they were placed in individual cages. The positive controls were maintained separately from the other groups. After nine months, the mice receiving 10 mg/kg in the diet dieldrin demonstrated palpable intra-abdominal masses, and by the fifteenth month, half the males and females in the group had died or had been killed when the masses became large. This period of 15 months is short compared to the 20 to 24 months that elapsed before one-half of the control group had died. The life spans of members of the 0.1 mg/kg and 1.0 mg/kg groups were similar to those of the controls. All the ADAB mice were dead by the 15th month.

An increased number of liver tumors was observed at all the concentrations of dieldrin including 0.1 mg/kg, with the highest increase occurring in the 10 mg/kg group. The tumors were classified by the authors as type (a) "...solid cords of closely packed parenchymal cells with a morphology and staining affinity little different from the rest of the parenchyma" or (b) "...areas of cells proliferating in confluent sheets and often with foci of necrosis. These lesions were distinguished from the previous types of growth by the presence of areas of papilliform and adenoid formations of liver cells with wide and irregular vascular channels within the growth." This classification appears somewhat arbitrary. Nonetheless, the presence of tumors was dose-related and effects were detected at the lowest dieldrin level tested (0.1 mg/kg). In addition to the increase in hepatic tumors there was an increase in the incidence of tumors at other sites.

In the second part of the Walker, et al. (1972) study, groups of 30 male and 30 female CF1 mice received ethylene oxide-sterilized diets containing 1.25, 2.5, 5, 10, or 20 mg/kg dieldrin for 128 weeks. The control group consisted of 78 males and 78 females and the conditions and observations were similar to those in the first experiment. In this part of the study, the mice that received 20 mg/kg dieldrin in the diet had a high mortality rate. About 25 percent of the males and 50 percent of the females showed signs of intoxication and died during the first 3 months. Liver masses were detected at 36 weeks, and all the mice either died or were killed at 12 months. Masses were not detected until 40 weeks in the 10 mg/kg mice, 75 weeks in the 5 mg/kg mice, and 100 weeks in the 2.5 mg/kg mice. In the 10 and 20 mg/kg groups, few animals were available for examination due to the acute toxicity or their being used in another study. The 5 mg/kg group had a higher incidence of tumors than the 2.5 mg/kg group.

The third part of the study was carried out under similar conditions. Groups of 60 mice received gamma-irradiated diets containing 0 or 10 mg/kg/diet dieldrin for 120 weeks. Also, groups of 48 mice received gamma-irradiated diets and litter for 110 weeks or unsterilized diets and litter for 104 weeks. The authors stated that liver enlargement occurrence and mortality were similar to those of the previous study.

The next section of the Walker, et al. (1972) study concerned the combined effect of dieldrin and DDT treatment on CFl mice. Initially, the mice were fed diets containing 200 mg/kg DDT or 10/200 mg/kg dieldrin/DDT. This resulted in high mortality. The diets were subsequently reduced to 50 and 100 mg/kg DDT and 5/50 mg/kg dieldrin/DDT. There were 47 males and 47 females in the control group and 32 males and 32 females in each of the treatment groups. In mice on the 5/50 mg/kg diet and 100 mg/kg DDT diet, liver enlargements were detected after 65 weeks of exposure. Both of these doses were toxic to males but only the 5/50 mg/kg dose was toxic to females. At 50 mg/kg DDT, masses were detected by the 96th week but the mortality was similar to that of the controls. In this experiment, the highest incidence of liver tumors was in the dieldrin/DDT group. However, because only one combination was tested, it is difficult to determine whether the effect was synergistic or additive. In a re-evaluation of the experiment, Reuber (see Epstein, 1975a,b, 1976), believes that Walker, et al. (1972) over-estimated the incidence of liver tumors in the control and DDT groups, thus minimizing the effect of the combined dieldrin/DDT.

In the last section of the Walker, et al. (1972) study, groups of 58 mice were fed dieldrin at 10 mg/kg for 2, 4, 8, 16, 32, and 64 weeks and sacrificed after 2 years. The control group consisted of 156 mice. All groups were equally divided between males and females. In the mice receiving dieldrin for 64 weeks, liver enlargements were detected after 60 weeks in six males and two females. These enlargements remained after the termination of the feeding. No other enlargements were detected and the mortality of all the groups was similar throughout the 2 years. It is important to note that type b tumors were detected after only 4 or 8 weeks of treatment and that the liver enlargements did not appear after the feeding was terminated.

A similar study of dieldrin and other chemicals in CF1 mice was carried out by the same group (Thorpe and Walker, 1973). The treatment groups were comprised of 30 males and 30 females and the controls of 45 mice of each sex. Dieldrin was tested at one concentration (10 mg/kg/diet) only, and the animals were not sacrificed when abdominal masses were large as in the previous studies. The study was terminated after 100 weeks of feeding. The authors reported that there were no signs of intoxication in the dieldrin groups; however, mortality increased after 22 months of exposure. Also liver enlargements were detected in both sexes by the 50th week. In this study, the cumulative tumor incidence and the number of dead mice were given at 17, 21, 25, and 26 months. Dieldrin at 10 mg/kg produced a high incidence of liver tumors. All the males and one-half the females that had died by 17 months had liver tumors. By the end of the study, 100 percent of the males and 87 percent of the females had liver tumors.

In a recent evaluation of both aldrin and dieldrin by the National Cancer Institute, aldrin and dieldrin were found to produce hepatic carcinomas in male mice. Female mice responded to low doses of dieldrin, but showed no effects from aldrin. No carcinomas were observed in either male or female rats of two different species (43 FR 2450 when the subjects were exposed to both aldrin and dieldrin. In the study on mice, groups of 50 male and 50 female $B_6C_3F_1$ mice were fed either aldrin (technical grade) or dieldrin (technical grade) at various doses. The females received aldrin at 3 and 6 mg/kg/diet and the males received aldrin at 4 and 8 mg/kg. Both sexes were given dieldrin at 2.5 and 5 mg/g. Aldrin controls consisted of 20 untreated males and 10 females and dieldrin controls had 20 animals per group. In addition, pooled controls consisted of 92 males and 78 females. The animals were fed the pesticide diets for 80 weeks and then observed for 10 to 13 weeks. All survivors were killed at 90 to 93 weeks.

In the male mice administered aldrin, there was a significant, dose-related increase in the incidence of hepatic carcinomas. The values were: matched controls 3/20 (15 percent); pooled controls 17/92 (19 percent); 4 mg/kg 16/49 (33 percent); and 8 mg/kg 25/45 (56 percent). The mean body weights of the aldrin- and dieldrin-fed mice were similar in the control and treated groups. There was a dose-related mortality in female mice at the high dose of aldrin. With the male mice fed dieldrin, a significant increase in hepatic-carcinomas was observed in the 5 mg/kg group. The incidences were 12/50 (24 percent) for the 2.5 mg/kg group and 16/45 (36 percent) for the 5 mg/kg group.

There have also been six carcinogenicity studies of aldrin and/or dieldrin done in various strains of rats. In an early paper by Treon and Cleveland (1955) aldrin and dieldrin were fed to male and female Carworth rats at 2.5, 12.5, and 25 mg/kg. The authors reported a significant increase in mortality and an increase in liver-to-body weight ratios at all concentrations tested. No data on tumor incidences were given, although some liver lesions were detected.

Later Cleveland (1966) summarized the work on aldrin and dieldrin conducted at the Kettering Laboratory. Although little data and details were given, Cleveland stated that aldrin and dieldrin were not tumorigenic in their rat studies.

A study was carried out by the U.S. Food and Drug Administration on aldrin and dieldrin in rats and dogs (Fitzhugh, et al. 1964) to determine the toxicity of these pesticides. Groups of 12 male and 12 female Osborne-Mendel rats were fed diets containing either aldrin (99+ percent purity) or dieldrin (100 percent purity) at 0, 0.5, 2, 10, 50, 100, or 150 mg/kg for two years. The animals were housed individually and the survivors were killed after two years. None of the dose levels of aldrin or dieldrin affected the growth of the rats but both chemicals at 50 mg/kg or greater reduced the survival. A significant increase in liver-to-body weight ratios was observed in both males and females for several doses of both chemicals. The authors reported no increase in liver tumors; however, there was a high incidence of multiple site tumors at lower concentrations of both aldrin and dieldrin.

Deichmann, et al. (1967) carried out a study in which 5 mg/kg aldrin (technical grade) was fed to male and female Osborne-Mendel rats, either individually or in combination with 200 mg/kg aramite, 200 mg/kg DDT, and 1000 mg/kg methoxychlor. There were 30 males and 30 females in each treatment group and they were housed in pairs. No increase in mortality over the controls was observed in any of the treated groups. Aldrin alone had no significant effect on liver-to-body weight ratio, but an increase in the ratio was noted in the groups treated with the pesticide mixtures. The authors state that one-half (13 females and 2 males) of the aldrin-treated rats had one tumor; however, only the tumors in survivors were listed.

Walker, et al. (1969) fed dieldrin (99+ percent purity) to Carworth rats at concentrations of 0, 0.1, 1.0, and 10 mg/kg in the diet for two years. There were 25 males and 25 females in each treatment group and 45 rats of each sex in the control group. The animals were housed individually and dying animals were killed and examined. The authors reported that some irritability, tremors, and convulsions occurred after two to three months but that the animals remained in good health for the two years. None of the dieldrin doses had any effect on body weight. Mortality was the same for the control and treated groups; however, all the groups had an overall, high rate of mortality. This resulted in only a few animals being available for examination at the conclusion of the feeding. At 1 and 10 mg/kg there were increases in liver-to-body weight ratios. Only one male rat and four female rats at the 10 mg/kg level demonstrated any liver cell changes. However, at the 0.1 and 1.0 mg/kg levels there were high but not significant increases in total tumors even though few animals were examined histologically.

In another study with the Osborne-Mendel rat, Deichmann, et al. (1970) examined aldrin, dieldrin, and endrin in a lifetime exposure. Aldrin (technical, 95 percent) and dieldrin (technical*, 100 percent active ingredients) were fed in the diet to groups of 50 males and 50 females. The concentrations during the first two weeks were 10, 15, and 25 mg/kg aldrin and 10, 15, and 25 mg/kg dieldrin. After this time all the dose concentrations were doubled for the remainder of the treatment time. The control groups contained 100 rats of each sex. Any animals that appeared ill were sacrificed. Both aldrin and dieldrin produced some dose-related toxicity, tremors, and clonic convulsions, especially in females. However, these doses had no effect on mean gain in body weight although some animals had marked loss of weight. The mean survival rate was somewhat lower in the aldrin and dieldrin rats; again, predominantly in females receiving the high concentrations. There were significant increases in liver-to-body weight ratios in males fed aldrin at 30 and 50 mg/kg and dieldrin at 30 mg/kg and a significant decrease in liver-to-body weight ratios in females fed aldrin at 20 mg/kg. A moderate increase in hepatic centrilobular cloudy swelling and necrosis was observed in both male and female rats fed aldrin and dieldrin as compared to the controls. However, there was no increase in the number of liver tumors or other site tumors. In fact, a decrease in total tumors was observed in both the males and females fed aldrin and dieldrin. The authors stated that this was possibly due to increased microsomal enzyme activity. It should be noted that limited re-evaluation of this data was carried out by Reuber who disagreed with the findings of Deichmann, et al. (1970). However, he re-evaluated only one group (dieldrin, 30 mg/kg) and there has been no independent re-evaluation of the material.

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*This is somewhat contradictory since "technical" dieldrin is actually 85 percent pure.

A two-year study by the National Cancer Institute (1976)(43 FR 2450) studied the effects of technical grade aldrin and dieldrin on Osborne-Mendel and Fisher 344 rats. The first part of the study used groups of 50 Osborne-Mendel rats of each sex for aldrin (30 or 60 mg/kg) and dieldrin (29 or 65 mg/kg). Aldrin was fed to the males for 74 weeks. The rats were then observed for an additional 37 to 38 weeks. All survivors were killed at 111 to 113 weeks. The same doses of aldrin were administered to the female rats for 80 weeks, followed by 32 to 33 weeks of observation. All survivors were killed at 111 to 113 weeks. The dieldrin rats were treated for 59 weeks at 65 mg/kg followed by 51 to 52 weeks of observation, or 80 weeks at 29 mg/kg followed by 30 to 31 weeks of observation. All survivors were killed at 110 to 111 weeks. For both pesticides, the controls consisted of 10 untreated rats of each sex plus pooled controls consisting the matched control groups combined with 58 untreated males and 60 untreated females from similar bioassays of other chemicals.

During the first year of the rat studies, the mean body weights for the aldrin-and dieldrin-fed rats did not differ from those of the controls. However, during the second year, the body weights of the treated rats were lower than those of the untreated. For both aldrin and dieldrin, no significant increase in hepatic carcinomas was observed in either sex. There was a significant increase in adrenal cortical adenoma in the low-dose aldrin- and dieldrin-treated female rats.

In the second part of the study on rats, 24 male and 24 female Fisher 344 rats were fed purified dieldrin at 2, 10, or 50 mg/kg for 104 to 105 weeks. Matched controls consisted of 24 rats of each sex. All survivors were killed at 104 to 105 weeks. The body weights of the treated and control rats were similar and survival was not greatly affected. The high-dose males and females demonstrated signs of intoxification at 76 and 80 weeks, respectively. A variety of neoplasms occurred in both the control and treated rats; however, there were no significant dose-related increases in the neoplasms.

There has been minimal work on the carcinogenicity of aldrin or dieldrin in dogs. A limited, short-term study was conducted by Treon and Cleveland (1955). Aldrin and dieldrin were fed to two male and two female beagles at 1 and 3 mg/kg/diet. The dogs were killed between 15 and 16 months. Although the growth rates of the treated dogs were similar to those of the controls, liver weights were increased at 1 mg/kg. These doses were toxic to the dogs and mortality was high. The study provides few data on the necropsy and the treatment was too short to adequately evaluate carcinogenicity.

In another study using dogs, Fitzhugh, et al. (1964) treated 26 animals with aldrin or dieldrin at dosages of 0.2 to 1.0 mg/kg/day, 6 days a week, up to 25 months. At doses of 0.5 mg/kg and greater, toxic effects including weight loss, convulsions, and death were observed. At 1 mg/kg/day or higher no animals survived over 49 days, and at 2.5 and 10 mg/kg/day all dogs died within 10 weeks. However, dogs fed 0.2 mg/kg/day of aldrin and dieldrin showed no ill-effects during the 2 years of the study. In the dogs fed aldrin at 1.0 mg/kg/day and dieldrin at 0.5 mg/kg/day, fatty degeneration was observed in the liver and kidneys. This study also w[illegible]oo short-termed to determine tumorigenic properties of aldrin and dieldrin. The number of animals surviving at the end of the study was inadequate to make any type of evaluation.

A third short-termed study on dieldrin in dogs was carried out by Walker, et al. (1969). Dieldrin (99+ percent purity) was administered to groups of five male and five female dogs in gelatine capsules at 0.005 and 0.05 mg/kg/day. After two years, the health and body weight of the treated dogs, as compared to the controls, was normal. A variety of physiological tests confirmed the general good health of the dogs. In dogs administered the higher concentration of dieldrin, liver-to-body weight ratios were increased significantly over the controls. The report stated that no lesions were seen in the tissues but provided no data on this.

There has been one report on the effects of dieldrin on Rhesus monkeys. The work of Zavon in 1970, which appears to be unpublished, has been summarized by Epstein (1975b). Epstein reports that six control monkeys (five male, one female) and groups of five monkeys each received 0, 0.1, 0.5, 1.0, and 1.75 mg/kg dieldrin in their diet for 5.5 to 6 years. The group at 1.75 mg/kg received 5.0 mg/kg for 4 months, then 2.5 mg/kg for approximatley 2.5 months, and then 1.75 mg/kg for the remainder of the exposure. Epstein further states that four of the monkeys died during the study, two of which had received 5 mg/kg. The remaining animals survived until they were killed. No data on histology are given although it is reported that no differences were observed between control and treated monkeys.

Versteeg and Jager (1973) summarized health studies carried out on pesticide workers in the Shell plant in Holland. These workers had occupational exposure to aldrin/dieldrin over periods of up to 12.3 years with a mean of 6.6 years. The average time that had elapsed from the end of exposure was 7.4 years (maximum, 16 years). The average age of the group was 47.4 years. The report states that 233 long-term workers were involved in this study and that no permanent adverse effects (including cancer) on the workers' health were observed.

Epstein (1975a) states that the epidemiological aspects of the study carried out by Shell have been reviewed by several experts who have criticized the study as inadequate due to the number of workers at risk and the short duration of exposure and/or time after exposure.

CRITERION FORMULATION

Existing Guidelines and Standards

Prior to 1974, aldrin and dieldrin were approved for use on 46 agricultural crops and for treatment of soil around fruits, grains, nuts, and vegetables (Int. Agency Res. Cancer, 1974a,b). In 1974 the registration of aldrin and dieldrin was suspended on the basis of adverse health affects in rodents (39 FR 37251). As a result, production is restricted for all pesticide products containing aldrin or dieldrin. Aldrin and dieldrin can no longer be used for spraying and dusting, or for mothproofing in which the residues are discharged into waterways. All uses in structures occupied by humans or livestock, uses upon turf, and any use involving application to any aquatic environment are also restricted. Aldrin and dieldrin can be used for termite treatment which involves direct application to the soil and therefore little movement of the pesticides. They may also be used for treatment of some non-food seeds and plant dipping during transplantation.

The current exposure level for both aldrin and dieldrin set by the Occupational Safety and Health Administration is an air time-weighted average (TWA) of 250 $\mu g/m^3$ for skin absorption (37 FR 22139). In 1969, the U.S. Public Health Service Advisory Committee recommended that the drinking water standards for both aldrin and dieldrin be 17 $\mu g/l$ (Mrak, 1969). Also, the U.N. Food and Agriculture Organization/World Health Organization's acceptable daily intake for aldrin and dieldrin is 0.0001 mg/kg/day (Mrak, 1969).

Current Levels of Exposure

The people of the United States are exposed to aldrin and dieldrin in air, water, and food. As mentioned earlier, aldrin or dieldrin has been found in more than 85 percent of the air samples tested by the U.S. EPA (Epstein, 1976). The levels were as high as 2.8 ng/m^3 resulting in an intake of up to 0.098 µg/day. Dieldrin can travel great distances in the air, especially when absorbed to particulate matter. Thus people can potentially be exposed to pesticide treatments from other countries.

Waters recently sampled in the United States contained aldrin or dieldrin in amounts up to 0.05 µg/l (Harris, et al. 1977). The standard diet in the United States has been calculated to contain approximately 43 ng/g of dieldrin. According to Epstein (1976) tolerances for dieldrin in cattle-meat fat, milk fat, meat, and meat by-products have been petitioned for at levels of 0.3, 0.2, and 0.1 ppm respectively.

Special Groups at Risk

Children, especially infants, have a high dairy product diet that has been shown to contain dieldrin (Manske and Johnson, 1975). It has also been demonstrated that human milk contains dieldrin residues and that some infants may be exposed to high concentrations of dieldrin from that source alone (Savage, 1976).

In early studies, Curley, et al. (1969) and Zarvon, et al. (1969) reported that dieldrin and several other chlorinated hydrocarbon pesticides were present in the tissues of stillborn infants. Curley, et al. also reported that dieldrin and other pesticides could be found in the blood of newborn infants.

No work has been carried out on neonatal animals with either aldrin or dieldrin; however, due to the sensitivity of neonatal animals to other carcinogens, this should be an area of great concern.

Basis and Derivation of Criterion

The aldrin and dieldrin carcinogenicity data of Walker, et al. (1972) and the National Cancer Institute (1976) were analyzed using a linear dose-response model to calculate that concentration of dieldrin in water which is estimated to result in an excess lifetime risk of 10^{-5} in man (see Appendix I). It should be noted that Walker, et al. study used 99 percent pure dieldrin while the NCI study used technical grade dieldrin.

Under the Consent Decree in NRDC vs. Train, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Both aldrin and dieldrin are suspected of being human carcinogens. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of aldrin/dieldrin in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of aldrin and dieldrin corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the Federal Register notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6} or 10^{-7} as shown in the table below.

Exposure Assumptions	Risk Levels and Corresponding Criteria (1)			
	0	10^{-7}	10^{-6}	10^{-5}
2 liters of drinking water and consumption of 18.7 grams of fish and shellfish (2)				
Aldrin	0	4.6×10^{-4} ng/l	4.6×10^{-3} ng/l	4.6×10^{-2} ng/l
Dieldrin	0	4.4×10^{-4} ng/l	4.4×10^{-3} ng/l	4.4×10^{-2} ng/l
Consumption of fish and shellfish only.				
Aldrin	0	4.6×10^{-4} ng/l	4.6×10^{-3} ng/l	4.6×10^{-2} ng/l
Dieldrin	0	4.5×10^{-4} ng/l	4.5×10^{-3} ng/l	4.5×10^{-2} ng/l

(1) Calculated by applying a modified "one hit" extrapolation model described in the FR 15926, 1979. Appropriate bioassay data used in the calculation of the model are presented in Appendix I. Since the extrapolation model is linear

to low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

(2) 99.9 percent of aldrin exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 4500 fold. The remaining 0.1 percent of aldrin exposure results from drinking water.

Ninety-eight percent of dieldrin exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 4500 fold. The remaining 2 percent of dieldrin exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of aldrin/dieldrin, (1) occurring from the consumption of both drinking water and aquatic life grown in water containing the corresponding aldrin/dieldrin concentrations and, (2) occurring solely from the consumption of aquatic life grown in the waters containing the corresponding aldrin/dieldrin concentrations.

Although total exposure information for aldrin and dieldrin is discussed and an estimate of the contributions from other sources of exposure can be made, this data will not be factored into the ambient water quality criteria formulation because of the tenuous estimates. The criteria presented, therefore, assume an incremental risk from ambient water exposure only.

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APPENDIX 1

Summary and Conclusions Regarding the Carcinogenicity of Aldrin and Dieldrin*

Aldrin has induced liver tumors in males and females of three strains of mice according to reports of four separate chronic feeding studies. It has failed to induce a statistically significant carcinogenic response in rats at any site according to reports of five studies in two different strains. In two bacterial assays with and without activation (S. Typhimurium and E. Coli) it was found to be non-mutagenic, but it did produce unscheduled DNA synthesis in human fibroblasts with and without activation. The induction of hepatocellular carcinoma in both male and female mice from the administration of aldrin leads to the conclusion that it is likely to be a human carcinogen.

Dieldrin, which is readily formed from aldrin in the environment and by metabolism of aldrin in rats, mice, fish, and many other species, has produced liver tumors in four strains of mice according to six reports of chronic feeding studies and possible liver tumors in an unpublished study with a fifth strain. In rats it has failed to induce a statistically significant excess of tumors at any site in six chronic feeding studies in three strains. It was found to be mutagenic in S. typhimurium after metabolic activation with mouse liver enzymes, but it was not mutagenic in two other studies of the same bacterial strain with a rat liver enzyme activation mixture. The induction of hepatocellular carcinomas in mice leads to the conclusion that dieldrin is likely to be a human carcinogen.

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*This summary has been prepared and approved by the Carcinogens Assessment Group, U.S. EPA, on July 25, 1979.

Both aldrin and dieldrin have been found to be non-mutagenic in several test systems as follows: a) gene conversion in S. cerevisie; b) back mutations in S. marcescens and c) foward mutations at two loci in E. coli. Several other organochlorine pesticides which produce mouse liver tumors are also non-mutagenic in the same systems.

The induction of liver tumors in mice of both sexes by aldrin and dieldrin is sufficient evidence that they are likely to be human carcinogens.

The water quality criterion for aldrin is based on the hepatocellular carcinoma incidence in male B6C3F1 mice of the low dose group in the NCI chronic test, and on the response in the 0.1 ppm group of female CF-1 mice in the Walker, et al. (1972) experiment (because aldrin in converted to and stored as dieldrin in fish). It is concluded that the water concentration of aldrin should be less than 4.6×10^{-2} ng/l in order to keep the lifetime cancer risk below 10^{-5}. For dieldrin the criterion is based on the response in the 0.1 ppm group of female CF-1 mice in the Walker, et al. (1972) experiment. The corresponding concentration for dieldrin is 4.4×10^{-2} ng/l.

Summary of Pertinent Data for Aldrin

The water quality criterion for aldrin is derived from the hepatocellular carcinoma response of the B6C3F1 male mice given the low dose of aldrin in the NCI bioassay test, and on the response in the 0.1 ppm group of female CF-1 mice in the Walker, et al. (1972) experiment. In the NCI study, a time-weighted average dose of 4 ppm was given in the feed for 80 weeks and the animals were observed for an additional 10 weeks before terminal sacrifice. The incidence of hepatocellular carcinoma was 3/20 and 16/49 in the control and treated groups, respectively. The slope of the one-hit dose-response curve for aldrin is calculated from the following parameters:

$n_t = 16$ Le = 90 weeks

$N_t = 49$ le = 80 weeks

$n_c = 3$ d = 4 ppm x 0.13 = 0.52 mg/kg/day

$N_c = 20$ L = 90 weeks

w = 0.035 kg

With these parameters the slope of the one-hit dose-response curve for aldrin is 6.349 $(\text{mg/kg/day})^{-1}$.

The conversion of aldrin to dieldrin in fish results in the accumulation of dieldrin residues in fish exposed to aldrin. This makes it necessary to consider the risk resulting from intake of dieldrin stored in fish due to the presence of aldrin in water. Thus, the criterion for aldrin also depends upon the one-hit dose-response curve for dieldrin, which has a slope of 183.6 $(\text{mg/kg/day})^{-1}$ as calculated previously from the Walker, et al. (1972) study.

The equation describing the risk due to aldrin in water is derived from the general relationship

$$P = B_H D \quad \text{and} \quad D = I/70\ \text{kg}, \quad \text{thus}$$

$$P = B_H\ I/70\ \text{kg} \quad \text{and}$$

$$P(70\ \text{kg}) = B_H I$$

where

P = individual lifetime risk (set at 10^{-5} for criterion calculation)

I = average daily human intake of the substance in question

B_H = estimated slope of the human one-hit dose-response curve

70 kg = average weight of humans

Since aldrin in water leads to the accumulation of dieldrin residues in fish, the equation describing the risk due to aldrin is

$$Pa\ (70\ \text{kg}) = B_{Ha}\ C_a\ (2.0\ \text{l/day}) + B_{Ha}\ C_a\ R_{ad}\ (0.0187\ \text{kg/day}) + B_{Hd}\ C_a\ R_{ad}\ (0.0187\ \text{kg/day})$$

where

P_a = risk due to aldrin (set at 10^{-5} for criterion calculation)

B_{Ha} = 6.349 $(\text{mg/kg/day})^{-1}$, the aldrin dose-response slope

B_{Hd} = 183.6 $(\text{mg/kg/day})^{-1}$, the dieldrin dose-response slope

C_a = criterion concentration for aldrin (to be calculated)

R_a = 32 l/kg, the fish bioconcentration of aldrin from aldrin

R_{ad} = 4468 l/kg, the fish bioconcentration of dieldrin from aldrin

2.0 l/day = average daily intake of water for humans

0.0187 kg/day = average daily intake of fish for humans

The term containing R_{ad} represents intake of dieldrin resulting from the presence of aldrin in the water, and is thus multiplied by the dieldrin dose-response slope. R_{ad} is estimated by assuming that in the absence of conversion to dieldrin, aldrin would bioconcentrate 4500 times (as dieldrin does), and that since aldrin only accumulates 32 times, the remainder of the expected aldrin residues are being stored as dieldrin.

The result is that the water concentration of aldrin should be less than 4.6×10^{-2} ng/l in order to keep the individual lifetime risk below 10^{-5}.

5600
91

Summary of Pertinent Data for Dieldrin

The water quality criterion for dieldrin is based on the hepatocellular carcinoma response of the female CF-1 mice given 0.1 ppm of dieldrin continuously in the diet in the experiment of Walker, et al. (1972). In that group the incidence of type a and type b liver tumors in the 0.1 ppm group of females was 24 out of 90 animals, whereas in the controls it was 39 out of 297 animals. Assuming a fish bioconcentration factor of 4500, the parameters of the dose-response model are:

$n_t = 24$ $d = 0.1 \text{ ppm} \times 0.13 = 0.013 \text{ mg/kg/day}$
$N_t = 90$ $L = 132 \text{ weeks}$
$n_c = 39$ $w = 0.025 \text{ kg}$
$N_c = 297$ $R = 4500$
$Le = 132 \text{ weeks}$ $F = 0.0187 \text{ kg/day}$
$le = 132 \text{ weeks}$

With these parameters the slope of the one-hit dose-response curve for dieldrin is 183.6 $(\text{mg/kg/day})^{-1}$.

The result is that the water concentration should be less than 4.4×10^{-2} ng/l in order to keep the individual lifetime risk below 10^{-5}.